Flow Experiments in a Carotid Artery Bifurcation for Magnetic Drug Targeting

PIV, PC-MRI and LDA

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Abstract

Magnetic Drug Targeting could be used to cure atherosclerosis in the Carotid Artery. The idea of this method is that magnetized drug particles are added to the blood in the artery while applying a magnetic field at the location where the drugs is desired to enter the tissue. Therefore the concentration increases at the location of the atherosclerosis while minimizing the side effects in the rest of the body.

For the prediction of the amount of drugs entering the tissue it is necessary to accurately determine the flow profiles in the Carotid Artery. Since the geometry of the Carotid Artery is unique for each person, a cheap and fast method to accomplish flow profiles is demanded. Simulations using Computational Fluid Dynamics could meet these requirements.

To validate Computational Fluid Dynamics simulations, experimental velocity measurements in a model of a Carotid Artery Bifurcation were performed. Particle Image Velocimetry and Magnetic Resonance Imaging were performed in the Carotid Artery Bifurcation and Particle Image Velocimetry and Laser Doppler Anemometry were performed in a cylinder, wherefore an analytical solution is available.

The reproducibility of Particle Image Velocimetry results was tested by comparing the measurements with previous work. Three different measuring techniques were used. The Particle Image Velocimetry results in the Carotid Artery Bifurcation showed indeed similar results. In addition, the possibility of constructing a quasi-3D model of data from different planes was investigated. It was concluded that due to interpolations a significant amount of information is ignored when the data from different planes were combined.

Phase-Contrast Magnetic Resonance Imaging experiments were repeated with some recommended improvements implemented. Smoothness of the images has improved. Qualitatively the results show in general good agreement with the PIV results.

Finally, Laser Doppler Anemometry was tested as measuring technique to measure the flow in the Carotid Artery Bifurcation model. Therefore the technique was tested in a cylinder. In general the results show good agreement. Moreover, a high resolution could be obtained if the refractive conditions are of sufficient quality.
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Introduction

1.1. Magnetic Drug Targeting

Magnetic Drug Targeting (MDT) is a method to get drugs on exactly the desired location in the body. For example chemotherapeutic drugs are only taken up by tumour cells for 0.1%-1% [1]. The rest of the drugs are affecting the healthy tissue which can cause severe side effects. The idea of MDT is to magnetize drug particles with a size in the range of 30-300 nm [2] and bring them into the blood circulation. By applying a magnetic field, the drugs can be pulled into the tissue at the disease location, therefore minimizing the side effects. It has been demonstrated [3] that MDT spares the immune system in comparison with conventional chemotherapy. A schematic is shown in figure 1.1. The particles are made for example by filling polymer capsules or micelles with both drugs and magnetic materials [1]. Particles could also be coated to protect them from the human immune system, so that the particles have a longer circulation time in the body before they are removed [4]. Magnetic fields are desirable for directing therapeutics inside patients because they can penetrate deep into the body and are considered safe even up to very high strengths (8 Tesla in adults) [5]. The blood flow drag forces on a particle vary with its position in the blood vessel [1]. A particle at the vessel center-line will experience a higher blood velocity and hence a higher drag force, but a particle near the blood vessel wall will be surrounded by a near zero blood velocity. Thus a particle near the vessel wall will experience a much smaller drag force and can potentially be held by a much smaller magnetic force. Blood usually has a strong flow field. In order to get the particles on the disease location, it is very important to accurately know the blood flow field, as the particles will follow this flow field. For Magnetic Drug Targeting the important questions are:

1. Where will the particles be captured in the vessel wall?
2. How many of these particles will be captured?

Furthermore, the flow is pulsating due to the heartbeats. The flow through the Carotid Artery can be simulated using Computational Fluid Dynamics (CFD) software, which is a fast and cheap method compared to experiments. However, the CFD simulations must be validated by experiments to leave no doubt about its accuracy. This thesis focuses on verifying existing CFD models, the reproducibility of experiments and comparing results with analytical solutions by using physical flow measuring techniques.

1.2. Carotid Artery Bifurcation

The Common Carotid Artery (CCA) is a blood vessel coming directly from the heart. It supplies the head and neck with oxygenated blood. The artery bifurcates in the neck and forms the Internal Carotid Artery (ICA) and the External Carotid Artery (ECA), shown in figure 3.1. The Internal Carotid Artery supplies the brain with oxygenated blood and the External Carotid Artery brings oxygenated blood to the muscles in the face and to the skin. The location where the CCA splits is called the Carotid Artery Bifurcation. In this study a model of
1. Introduction

Figure 1.1: Schematic of blood vessel [1]. Blood and a constant concentration of magnetic nanoparticles enter from the left. The magnetic particles within the blood vessel experience diffusion, convection under blood flow, and magnetic forces. Magnetic particles in the surroundings experience diffusion and magnetic drift but no blood drag forces.

Figure 1.2: Atherosclerosis: Plaque of fatty material narrows the artery and hinders the blood to flow. [8]

A Carotid Artery Bifurcation is used to investigate the blood flow in this vessel. The model is obtained from a Computed Tomography (CT) scan of a patient suffering from atherosclerosis. The results could be used to apply Magnetic Drug Targeting.

1.2.1. Why this vessel?

Atherosclerosis is a disease of the arteries characterized by the deposition of plaques of fatty material on their inner walls. The plaque could build up where the arterial wall is damaged. The damage may be caused by smoking, high concentration fats or cholesterol in the blood, high blood pressure or high concentration of sugar in the blood [6]. The layer of fatty material narrows the artery and subsequently the blood is hindered to flow. Cardiovascular diseases are a heavy load on health care systems and government budgets [7]. In 2012 there were 1.9 million deaths in the European Union resulting from diseases of the circulatory system, which was equivalent to 37.9 % of all deaths. For comparison, cancer was in that year the second most prevalent cause of death, accounting for 25.8 % of all deaths. The Carotid Artery is an important blood supplier for the brain. Therefore atherosclerosis in the Carotid Artery is one of the main causes of brain damage. Magnetic Drug Targeting could be used in this artery to locally fight this plaque forming and prevent worse.
1.3. Research Questions

- Are Particle Image Velocimetry measurements in the Carotid Artery Bifurcation reproducible?
- Can the third dimension be added to the Particle Image Velocimetry measurements by measuring a perpendicular plane to obtain a third velocity component?
- Could previous Phase-Contrast Magnetic Resonance Imaging results be improved?
- Is Laser Doppler Anemometry a suitable measuring technique to measure the flow in the Carotid Artery Bifurcation model?
2.1. Flow Measurement Techniques

For Magnetic Drug Targeting it is necessary to accurately know the flow patterns to be able to position the drugs on the desired location. Each person has a specific Carotid Artery geometry and therefore the flow patterns will be patient-specific. The easiest way to determine the flow pattern is to make a Computer Tomography (CT) scan of a patient to obtain the precise geometry of the Carotid Artery and to use this geometry to perform Computational Fluid Dynamics (CFD) simulations of the blood flow. To verify the computer model, it is possible to measure the flow pattern with Phase-Contrast Magnetic Resonance Imaging (PC-MRI), an already widely used imaging technique in hospitals. However, this method is less accurate than other available measurement techniques. Therefore it is desired to compare PC-MRI results with flow patterns constructed by these other techniques.

2.1.1. Particle Image Velocimetry

Particle Image Velocimetry (PIV) is an optical technique to measure flow velocities. The basic principal is to measure the positions of particles along the flow at two different moments. The displacement of the particles in a certain time interval is a measure for the velocity of the particles. This technique is non-intrusive, which means that the flow will not be affected by the measurement. A big range of velocities can be studied by adjusting the time interval of measuring. One of the greatest advantages of the technique is the ability to measure hundreds or thousands of flow vectors simultaneously.

The particles could be naturally present in the fluid, which is called natural seeding [9], or the particles could be deliberately added to the fluid, called artificial seeding. For both method holds that the particles should accurately follow the flow dynamics. In addition, the particles should scatter sufficiently so that the particles can be seen on a CCD camera. Thus in order to capture the scattered light from the seeding particles on the camera, the fluid should be transparent. Tracer particles are typically hollow glass or polystyrene spheres with a diameter ranging [10] from 2 to 100 micrometer for aqueous fluids. In this study hollow glass spheres with a diameter of 8-12 micron are used. The particle density can highly influence the accuracy. To construct a flow field, the flow area captured on the camera is divided into small so-called interrogation areas. Each interrogation area will produce a vector. This results in a spatial-averaging effect on the correlated velocity vector field. One interrogation area is typically [11] in the range of 12x12-64x64 pixels. The smaller the interrogation cells the better the spatial resolution [10], however, if insufficient particles exist within each cell, the correlations can weaken by high frequency noise in the displacement estimates. The used algorithm uses decreasingly smaller interrogation cells such that a coarse velocity vector field is correlated using a specified number of correlation iterations with large interrogation cells (e.g. 64x64), subsequently, the vector field is refined by correlation iterations with interrogation cells which sides are half as large (e.g. 32x32) until the smallest specified interrogation cell size is reached. So an initial as well as a final interrogation window size must be specified. This technique is used to improve initial displacement estimates, by correlating more particle pairs in larger interrogation cells, such that smaller final interrogation cells may be used to increase
spatial resolution. At least 6 particles should be present in each frame or interrogation area. However, not more than 30 particles should be present in each interrogation area, as the particles become indistinguishable. The interrogation cells associated with a particular velocity vector could overlap the interrogation cells of neighboring velocity vectors. An overlap increases the spatial resolution significantly, e.g. a typical 50% overlap [12] increases the spatial resolution with 100%.

Several possibilities are available to measure the distance, for example using a relatively long exposure time such that the distance that the particles have travelled becomes visible. Another possibility is to make an image using two light flashes, showing the displacement of each particle. In this study a third method is used whereby two images are taken shortly after each other. A vector field can be obtained by performing a cross-correlation between the two images. This method provides the most accurate results and is relatively easy to use. The time between two images should not be too short, since no displacement can be observed. However, if the time is too long, the particles have travelled along with the flow out of the interrogation area and cross-correlation can not be performed anymore. Thus the optimal time depends on the velocity of the particles.

Light sources could be natural sunlight or a lamp, but mostly lasers are used. They can create a high light intensity which is very localized, with the help of some optical devices. A laser sheet with a thickness of approximately 1 mm is created using a cylindrical and a spherical optical lens. A wavelength of 532 nm is used,
which is in the visible light regime and therefore safer. Particle Image Velocimetry is schematically shown in figure 2.1.

2.1.2. Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) is an imaging technique mainly used in hospitals to visualize patient's tissue without opening the body. It is based on nuclear magnetic resonance [13], which is caused by the angular momentum, or spin, of protons. Since protons are positively charged, moving protons will constitute a current. This electrical current will induce a magnetic field. Therefore, moving protons act like little magnets. The protons precess with a certain precession frequency, which depends on the external applied magnetic field. This angular frequency of a proton is described by the Larmor equation

$$\omega_0 = \gamma \cdot B_0$$  \hspace{1cm} (2.1)

where $\omega_0$ is the angular frequency, $\gamma$ is the gyromagnetic ratio and $B_0$ is the external magnetic field strength. The gyromagnetic ratio is the ratio of the magnetic dipole moment to its angular moment. This number is specific for each material. The orientation of the protons with respect to the magnetic field can be seen in figure 2.2. In the MRI scanner, strong magnets in the order of 1-7 Tesla cause a magnetic field. The protons follow the external magnetic field lines. If a nucleus consists of an odd number of protons, the nucleus has a net magnetization and is therefore suitable for MRI. The protons will be either parallel or anti-parallel to the magnetic field lines. The protons which align parallel are in a lower energy state. Few more protons are in the lower energy state. These protons form the net longitudinal magnetization, since the rest cancels each other out. However, it is not possible to measure this parallel magnetization.

To measure the magnetization, the longitudinal magnetization should be transformed in transversal magnetization, which is perpendicular to the external applied magnetic field. Therefore a short radio frequency (RF) pulse is sent in. If the protons and the RF pulse have the same frequency, the protons start to resonate. The RF pulse exchanges energy and causes some protons to go to a higher energy level, which is anti-parallel to the external applied magnetic field. The pulse also changes the phase of the protons so that they synchronize. As a consequence, the longitudinal magnetization decreases and a transversal magnetization arises. These are independent processes. Immediately after the RF pulse the protons start to return to their initial lower energy state. This is a continuous process called longitudinal relaxation. The time it takes to reach 63% of the original longitudinal magnetization is called the longitudinal relaxation time and is denoted by $T_1$. $T_1$ is about 300-2000 ms in biological tissues and depends on tissue composition, structure and surroundings. The transversal magnetization decreases and disappears, which is called transversal relaxation. The transversal relaxation time is the time when transversal magnetization decreased to 37% of its original value and it denoted by $T_2$. $T_2$ is in the range of 30-150 ms in biological tissues and depends on inhomogeneities of magnetic fields. The moving magnetic vector induces an electrical current in the antenna of the MRI scanner. A gradient in the magnetic field is applied to be able to distinguish positions. Processing of the signals enables a computer to construct an image and to distinguish between tissues.

So far the theory covers tissues in rest. In this thesis however the MRI scanner should measure flow velocities. Phase-Contrast MRI makes use of the spin of moving protons. Two gradients are applied, both with the same magnitude but in opposite direction, known as a bipolar gradient. This will cause no net effect for stationary spins. Moving spins however end up at a different position along the gradient with thus a different magnitude, causing a phase shift proportional to the velocity.

The used MRI scanner for the experiments is situated in LUMC Leiden, the Netherlands. This scanner has a magnetic field strength of $B = 3T$. To improve the signal, contrast could be added to the fluid. Air bubbles in the model between the PDMS and the perspex causes the magnetic susceptibility to be inhomogeneous and therefore distorting the MRI signal. A simple though effective trick to overcome this problem is to add some soap to the fluid.

A parameter that must be specified before performing a PC-MRI study is $VENC$ [15]. $VENC$ stands for velocity encoding. $VENC$, measured in cm/s, should be chosen to include the highest velocities likely to be encountered within the vessel of interest. If $VENC$ is set to 50 cm/s, for example, flows in the range of ±50
cm/s can be accurately represented by a set of phase shifts spanning from -180° to +180°. The VENC parameter adjusts the strength of the bipolar gradients so that the maximum velocity selected corresponds to a 180° phase shift in the data. The VENC setting is critical for proper performance of the PC pulse sequence, but usually can only be estimated since its optimal value is generally not known in advance. Often a study will be repeated using 2-3 different VENCs based on typical expected velocities. If the selected VENC is set too high, the range of flows imaged will span only a limited phase shift range. The signal-to-noise of the image and quality of the data will suffer. Small velocity differences on flow studies will not be distinguishable, and small flow velocities in certain vessels may be impossible to see. As a general rule, choosing VENC about 20 to 25% higher than the maximum expected flow velocity is advised.

2.1.3. Laser Doppler Anemometry

Laser Doppler Anemometry (LDA) is a velocity measuring technique for fluids and gases which makes use of the Doppler frequency shift of laser light scattered by a moving particle. LDA is also known as Laser Doppler Velocimetry (LDV). The technique takes advantages of the principle that if a moving particle crosses a beam of monochromatic light, it will cause a frequency shift \( f_d \) in the scattered light waves. This frequency shift is related to the velocity component of the particle velocity in the direction perpendicular to optical axes of the system. The measurement is based on the stability and linearity of optical electromagnetic waves, which can be considered unaffected by other physical parameters such as temperature and pressure. As with Particle Imaging Velocimetry, small particles should be added to the fluid or gas that are following the flow accurately. The natural flow pattern is not disturbed by the measurements, so this technique is also non-intrusive. A necessary condition is transparency of the set-up. The laser beams must be able to access the fluid. The quantity measured by the laser Doppler method is the projection of the velocity vector on the measuring direction defined by the optical system. Two beams of monochromatic light can distinguish between particles crossing the same beam at different locations. Moreover, the frequency shift caused by two beams is larger and therefore easier to measure. The intersection of the beams is called the measurement volume. A linear combination is formed from the scattered light from the two beams. The direction of the two beams differs and therefore the frequency shifts differ as well. The Doppler frequency of the scattered light is given by [16]

\[
f_d = f_2 - f_1 \approx \frac{v_x}{\lambda} \sin \theta
\]  

(2.2)

Where \( \lambda \) is the wavelength and \( \theta \) is the angle between the crossing beams. Since \( f_d \) is measured and \( \theta \) and \( \lambda \) are known, the velocity component can be determined. All three velocity components can be measured simultaneously by combining three different laser beam couples with different wavelength. When two co-
2.1. Flow Measurement Techniques

Figure 2.3: When two coherent laser beams intersect, they will interfere in the volume of the intersection. If the beams intersect in their respective beam waists, the wave fronts are approximately plane, and consequently the interference will produce parallel planes of light and darkness. The interference planes are known as fringes. [17]

Figure 2.4: LDA principle. The Bragg cell splits the light beam coming from the laser and adds a frequency shift. At the desired measurement point the laser beams cross. The light is scattered back by the seeding particles and is caught by the receiving optics. The resulting current contains the frequency information relating to the velocity to be measured. [17]

herent laser beams intersect, they will interfere in the volume of the intersection. If the beams intersect in their respective beam waists, the wave fronts are approximately plane, and consequently the interference will produce parallel planes of light and darkness as shown in figure 2.3. The interference planes are known as fringes, and the distance $\delta f$ between them depends on the wavelength and the angle between the incident beams, given by the relation

$$\delta f = \frac{\lambda}{\sin \frac{\theta}{2}} \quad (2.3)$$

Where $\lambda$ is the laser wavelength and $\theta$ is the beam crossing angle. Since $\delta f$ is constant for a given optical system, there is a linear relation between the Doppler frequency and velocity. The fringe spacing is therefore constant and is the calibration factor for the system, which should be specified in the software. The LDA requires no physical calibration since the fringe spacing is calculable from the optical parameters and unaffected by other changing variables in the experiment [17]. Advantages of LDA are fast signal processing and a small measurement volume and therefore the temporal and spatial resolutions are high. A disadvantage of LDA is that the velocity is measured in only one point. To construct a 2D or 3D velocity profile, a selection of points must be made. The higher the desired resolution, the more time consuming the method will be. The optical and dynamical properties of seeding particles are an essential element of LDA measurements. In general the signal increases with increasing particle size and an increasing difference in index of refraction. The size of the seeding particles is typically in the range of 1 $\mu$m [18].
2.2. Reynolds Number

The Reynolds number is a dimensionless number. It helps to predict flow behaviour.

\[ Re = \frac{\rho vD}{\mu} \tag{2.4} \]

where \( \rho \) is the density of the fluid, \( v \) is the average velocity of the fluid, \( D \) is the diameter of the tube and \( \mu \) is the dynamic viscosity of the fluid. The Reynolds number is the ratio of inertial forces to viscous forces. If the Reynolds number is high, inertial forces dominate and with a low Reynolds number viscous forces are dominant. By keeping the Reynolds number at the same value, a dynamically similar flow can be studied even though the model is scaled. In this study, realistic Reynolds numbers between 0 and 500 are studied. The Reynolds number is defined at the inlet of the Carotid Artery Bifurcation. The inlet diameter is known to be 16 mm. The flow meters measure the flow. The average velocity of the fluid can then be calculated. The viscosity of the fluid is measured using a rheometer and density is obtained by weighing a known volume.

2.3. Womersley Number

In arteries a non-constant pressure gradient is induced by the heart which results in a pulsatile behaviour. The Womersley number is a dimensionless number that represents the ratio of transient forces, originating from a pulse wave, to the viscous force and is defined as

\[ \alpha^2 = \frac{\omega R^2 \rho}{\mu} \tag{2.5} \]

where \( R \) is the radius of the pipe, \( \omega \) is the angular frequency of the oscillations, \( \rho \) is the density and \( \mu \) the dynamic viscosity of the fluid. The number is named after J.R. Womersley for his work on arterial mechanics. As for the Reynolds number, the same Womersley number accounts for dynamic similarity. The Womersley number in human arteries [19] [20] varies from 1-12.5.

2.4. Electromagnetic Flow Meters

Electromagnetic Flow Meters can be used to measure the flow rate of electrically conductive fluids. The physical principle behind the flow meters is Faraday’s law of induction. Two coils inside the flow meter generate a constant magnetic field over the entire cross section of the measuring tube. Two electrodes are installed at the wall of the tube at a right angle. The electrodes can pick up electrical voltages. The inner wall in the flow meter is insulated so that short circuits are prevented. If the charged particles of the conductive liquid flow through the magnetic field, the magnetic field applies a force at the charged particles. Consequently, the positively charged particles are separated from the negatively charged ones and collected on the opposite site of the tube wall. Now an electrical voltage forms, detected and measured by the two electrodes. This voltages is directly proportional to the flow velocity in the pipe line.

\[ U = kBDv \tag{2.6} \]

where \( U \) is the induced voltage, \( B \) is the magnetic field strength, \( D \) is the distance between the two electrodes, \( v \) is the velocity of the conducting liquid and \( k \) is a calibration factor. The magnetic field is alternately reversed to eliminate interference voltages. A flow-proportional frequency signal is provided as the output signal. A great advantage of this flow meter is that it is not obstructing the flow. The orientation should be such that the flow meter is completely filled with liquid. Typical accuracy of a magnetic flow meter [21] is 0.5% of the measured value from 0.1 to 10 m/s. The minimal conductivity of the medium should be at least 20 \( \mu \)S/cm since lower conductivity affects the accuracy. Typical drinking water [22] has a conductivity in the range of 50-500 \( \mu \)S/cm. Glycerol solutions with pure water [23] have a conductivity around 10 \( \mu \)S/cm.
2.4. Electromagnetic Flow Meters

Figure 2.5: Principle of an electromagnetic flow meter [24]. Two coils (in red and green) generate a magnetic field. The conductive fluid separates the negatively charged particles and the positively charged particles. The voltage that now has arisen is picked up by two electrodes (yellow) and is directly proportional to the liquid velocity. The electromagnetic flow meters in this thesis are used to calculate the Reynolds number with the determined flow.
3.1. Model of Carotid Artery Bifurcation

The patient specific Carotid Artery Bifurcation was manufactured by 3D-printing a digital geometry obtained with a Computer Tomography (CT) scanner from a patient suffering from atherosclerosis. The model was printed with wax. Subsequently the model was placed in a perspex housing which was filled up with polydimethylsiloxane (PDMS). After drying the wax model was casted in the PDMS and the wax was removed. The model was scaled up approximately 2.1 times of the original dimensions, leading to an inlet diameter of 16 mm. During fabrication, one of the arteries after the bifurcation was slightly moved. Therefore, the measurements can not overlay the CFD model perfectly. Moreover, the model has no elastic walls like a real human artery. More information about the fabrication can be found in reference [25]. Figure 3.1 shows a scan of the Carotid Artery Bifurcation. In this study, the lengthwise direction, i.e. the main flow direction is the x-direction.

3.2. Fluid

For each different measurement technique an appropriate fluid needs to be found. For the optical methods PIV and LDA the fluid must be transparent and the refractive index of the fluid must match the refractive index of the PDMS, so that the laser light is undistorted. For PC-MRI however, the fluid does not have to be transparent but a long relaxation time is desired that enables to pick up sufficient signal.

3.3. PIV Experiment

The PIV experiments have two major goals. A part of the experiments have been done before and therefore the first goal is to show that the experiments are reproducible. The second goal is to add a new dimension by measuring different planes.

3.3.1. Refractive Index Matching

PIV requires the model to be optically undistorted. Therefore it should be not only transparent, but the refractive indices of the PDMS and the fluid should be matching as well. The refractive index of PDMS is known to be 1.413. Several options are available to find a fluid with this refractive index. One of them is pure liquids with the same refractive index, for example oils. Another option is to use an aqueous solution. Previous research concluded that a glycerol solution is the best option since it is stable in time, save, inexpensive and it matches refractive index sufficient. In a timescale of weeks, only some water has evaporated and was added again. However, the viscosity is quite high and therefore it is more difficult to obtain higher Reynolds numbers. The refractive index of perspex is not matching, however, the laser light will incident perpendicular to the surface and therefore the light beam will not be refracted.
In previous research the glycerol solution is used as well and turned out to be a sufficient working fluid, therefore it was chosen to use a glycerol solution in this study as well. The concentration of the glycerol was varied until a refractive index of 1.4130 was obtained. The refractive index was measured using a Zeiss Opton Refractometer 121217. Before obtaining good result the phantom must be cleaned. Contamination of old seeding particles at the wall of the Carotid Artery Phantom can cause non-transparency, even though the refractive index is matching. The images of the phantom with different fluids and the refractometer are shown in figure 3.6.

3.3.2. Density & Viscosity

For calculating the Reynolds number and Womersley number, the density and the viscosity must be known. The density is obtained by weighing a known volume of the eventual glycerol solution using a weighing scale. The density turned out to be 1180 kg/m$^3$. The viscosity was measured using a rheometer which obtained a value of 0.00925 Pa·s at 25°C.

3.3.3. Flow Cycle

Steady flow as well as pulsatile flow were measured. The flow cycle is shown schematically in figure 3.3. In the steady flow case, an aquarium pump is used to pump the fluid through the system. The aquarium pump is directly placed in a reservoir. Due to dissipation of the pump, the fluid can slightly heat up. To prevent this temperature rise from influencing the viscosity and thus the Reynolds number, a thermostatic bath is installed. Herein the fluid flows through a metal spiral pipe which is placed in a water bath held at a constant temperature of 25°C. Air can be removed manually from the system by an outlet pipe. Then the fluid goes through the phantom. The outflow ratio of the Internal Carotid Artery (ICA) and the External Carotid Artery (ECA) to the Common Carotid Artery (CCA) can be regulated by two valves. These valves control the outflow ratio by applying resistance on the flow. In a real body, resistance is caused by arteries and capillaries. The
3.3. PIV Experiment

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<th>VAD Settings</th>
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<td>Psys</td>
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<td>Volume</td>
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Table 3.1: The settings for the Ventricular Assist Device. The same settings were used as in the reference thesis [9]. The VAD is used univentricular; only the left VAD is used (LVAD).

outflow ratio ICA/CCA is approximately 0.65 and the outflow ratio ECA/CCA is approximately 0.35 in a patient without atherosclerosis [26]. The arteries are shown in figure 3.1. In this experiment with an artery from a patient that is suffering from atherosclerosis, two outflow ratio’s 50/50 and 60/40 are applied. The two valves are both followed by an electromagnetic flow meter. These flow meters are connected directly to a computer to accurately determine the outflow ratio. Adjusting the outflow ratio goes manually. Finally, the fluid returns to the reservoir. For steady flow, Reynolds numbers of 82 and 189 are studied. The intention was to use higher Reynolds numbers, however, after analysing, the assumed Reynolds numbers had to be revised. To obtain certain Reynolds numbers, the power of the aquarium pump must be manually adjusted to set the velocity. For a Reynolds number of 82, the equation becomes

$$Re = \frac{\rho v D}{\mu} = 82 \quad (3.1)$$

For an inlet diameter of 16 mm, a density of 1180 kg/m³ and a dynamic viscosity of 0.00925 Pa · s the average velocity at the inlet should be 0.04 m/s. For a Reynolds number of 189, the equation becomes

$$Re = \frac{\rho v D}{\mu} = 189 \quad (3.2)$$

The average velocity at the inlet should be 0.0925 m/s.

In case of pulsatile flow measurements, the VAD is used. A VAD is a mechanical pump that is used to support heart function and blood flow in people who have weakened hearts. Normally, the device takes blood from a lower chamber of the heart and helps to pump it to the body and vital organs, just as a healthy heart would do. For PIV however, a transparent fluid such as water or glycerol is used.

A measured amount of compressed air delivered through a pneumatic line compresses the ventricular chamber. Diastolic pump filling is achieved by negative pressure suction. Negative pressure allows for complete filling. The diastolic settings range from -99 mmHg to -1 mmHg. Systolic drive pressures range from +50 mmHg to +300 mmHg. So the power source generates positive and negative pressures to move the membrane that separates a blood chamber from an air chamber. In case of insufficient filling of the VAD (the VAD diastole) the vacuum pressure could be decreased, so the pressure should be more negative. Also, the VAD rate could be lowered to allow for sufficient filling. In case of insufficient emptying of VAD (the VAD systole) the systolic driving pressure could be increased. Only the left part of the heart is mimicked. The right part of the heart receives blood with a low oxygen level and pumps it to the lungs. The left part of the heart receives the oxygenated blood from the lungs and pumps it to the aorta, which leads the blood to the organs. In case of the Carotid Artery Bifurcation, oxygenated blood from the heart is flowing through. It is possible in real patients to take over both left and right parts of the heart, however, two pumps are needed in this case, as can be seen in figure 3.2.

The VAD is pumping the glycerol solution from a reservoir into the system with 40 beats per minute. This value is quite low, however, increasing this value will cause the VAD to be not completely filled before contraction and thus the flow rate will not reach the desired values. The flow rate that goes into the system is regulated by a valve. The Womersley number is

$$\alpha = \sqrt{\frac{\omega R^2 \rho}{\mu}} = 5.8 \quad (3.3)$$

The angular frequency is $2\pi f$ with $f=\frac{2}{3}$ Hz, the radius is again the radius of the long inlet, which is 8 mm.
3.3.4. Laser

For the Particle Image Velocimetry experiment, a pulsating laser system is used that emits laser light with a wavelength of 532 nm. This wavelength is in the visible light regime and is therefore considered as safer than non-visible laser light. The wavelength corresponds to the color green. A sheet is focused at the phantom. Two pulses shortly after each other illuminate the tracer particles. These pulses are generated by two different lasers of which the beams should follow the same path. The two lasers are necessary because one single laser is not able to generate these pulses after each other in such a short period of time. For technical reasons, the first pulse is shorter than the second. If the laser beams do not follow the same path, the two sheets do not illuminate the same location in the flow and PIV can not be performed. In this case the laser beams should be aligned.

After the beam leaves the laser, the path’s direction is changed 90° by a mirror. Subsequently, a plano-concave lens turns the beam into a sheet. A biconvex lens focuses the sheet at the desired location, so that the sheet is as thin as possible at the measuring location. The sheet is not of the same thickness everywhere, but it is known to be approximately 1 mm in the area of measuring. The power of the laser does not exceed the laser damage threshold. The laser pulses are 15 mJ each and have a maximum frequency of 15 Hz. The release of the laser beam consist of two parts. The flashlamp excites the beam and the Q-switch releases the beam. The path of the laser light is shown in figure 3.4.

The used camera is the Lavision Imager Intense, which belongs to the PIV software Davis from Lavision. The focal length is 28 mm. The aperture can be varied from 1.3 to 10 mm in diameter. Basically as much light as possible is desired, but overexposure must be avoided. The optimum aperture turned out to be 5 mm (this is aperture number 28/5 = 5.6). By comparing the two subsequent images, the displacement of the particles is determined. From the displacement in a certain time step a velocity profile is made visible. This time step is manually chosen and must depend on the velocity. If the velocity is low, the dt must be chosen larger so that the particles have moved. However, the dt must not be too large, since the particles should not move outside the interrogation area. Post-processing will then fail. To obtain a reliable velocity profile, multiple measurements are averaged. For steady flow the frequency of the measurements can be equal to the highest frequency of the laser since this will cost less time. For pulsating flow, the frequency of these pulses is adjusted to the frequency of the VAD, because the measurements must be taken at exactly the same moment in the pulse cycle. The eventual flow field is an average over 25 measurements.
3.3.5. Dimensionality

PIV is a two-dimensional method to obtain a flow field. The third dimension is added in each set of measurements by dividing the phantom into slices of 1 mm, because the laser sheet as a thickness of approximately 1 mm. During post-processing these slices are added and so a quasi 3-dimensional structure is constructed. However, if the velocity vectors are measured in the x-y plane, the z-component has not been measured and is set to zero. If the velocity vectors are measured in the x-z plane, the y-component has not been measured and is set to zero. It has been considered to add the z-component of the velocity measured in the x-z plane to the x-y plane measurements to have the velocity vectors in all directions. However, for the x-y plane measurements only 24 z-planes or 'slices' of 1 mm are measured. As a consequence, only 24 z-velocity vector components can be added for each x-y pair. Therefore the z-velocity vector components must be discretized and averaged. In other words, the same value should be given to all the y-positions within one slice. Similarly, only 39 x-z planes are measured and therefore only 39 different y-planes are available to match a z-velocity component. The y-component in the x-y measurements must be discretized by dividing the y-axis into 39 parts. Due to these interpolations the error would become too large. Therefore it is decided that the measurements are not combined but showed separately.
3.4. MRI Experiment

For the MRI experiment the same model of the Carotid Artery Bifurcation was used. MRI does not require the model to be optically undistorted. Since previous MRI experiments with glycerol showed poor contrast, it was decided to use water instead. This came with new difficulties as the viscosity and density are very different for water than for glycerol. To maintain the same Reynolds number the flow had to be decreased drastically to about 0.2 L/min, but the new flow rate was not in the range of the used magnetic MAG VIEW MVM 005 Q flow meters, which are suitable for flows between 0.25 and 5 L/min according to the specifications. This range is quite large and therefore the flow meters had to be calibrated for such low flow rates. The voltage is then adjusted to the flow rate. If the flow rate is relatively low, it is not necessary to use the whole range of the flow meter. In fact, this will only decrease the accuracy. Therefore a maximum velocity was set to decrease the range. For example: if the measured flow rate is about 0.8 L/min, the maximum velocity can be set at 1 L/min, so that in the range 0-1 L/min the flow rate can be measured more accurately. To measure the 1 L/min, the volume or weight of the pumped fluid in a certain time interval can be measured. However, the flow rate that had to be measured was below the range of the flow meters. Therefore it was difficult to measure the flow accurately. Moreover, the low flow rates were very hard to accurately adjust using the mechanical valves. So eventually it was decided to measure the flow and the outflow ratio using the MRI measurements. The suitable VENC (velocity encoding) settings were found by trial and error. For the 50/50 outflow ratio measurements VENC 20 turned out to be the most appropriate while for the 60/40 outflow measurements VENC 15 was the best setting.

To improve signal, contrast was added to the working fluid. From experience 1 ml of contrast per liter of fluid should work well. It was estimated that the total volume in the system was around 60 liters. During filling of the system lots of small air bubbles got stuck onto the inner wall of the tubing and of the phantom as
### Fluid Properties

<table>
<thead>
<tr>
<th>Substance</th>
<th>Density</th>
<th>Viscosity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>1000 kg/m³</td>
<td>$10^{-3}$ Pa·s</td>
</tr>
</tbody>
</table>

Table 3.3: Properties of the working fluid used for Magnetic Resonance Imaging.

Figure 3.5: LDA set-up. An aquarium pump leads the water through the cylinder. The transmitter emits four beams, two in the vertical direction and two in the horizontal direction. The cross-section of the cylinder is scanned using a traverse that moved the whole system over the diameter of the cylinder, here indicated as a dotted line. With the velocity vectors in each discrete point a Poiseuille flow profile should appear. Tracer particles in the fluid scatter back light to the receiver. The photo detector converts the optical signals to electronic signals for the signal processor.

well. To overcome this problem a bit of soap was added to the fluid and the bubbles vanished very fast. The measurements were performed in a 3 Tesla MRI scanner in the LUMC hospital in Leiden. In the MRI room, no metal is allowed because of the magnetic field of the scanner. Therefore only the phantom was located inside the room. Long tubing (of about 10 m) through a hole in the wall connected the phantom with the rest of the set-up. The experimental set-up is shown in figure 3.8.

### 3.5. LDA Experiment

The third velocity measuring technique used for this thesis is Laser Doppler Anemometry which makes use of the frequency shift of two reflected laser light caused by the velocity of a tracer particle. LDA requires the model to be optically undistorted just as PIV. Therefore the set-up should be not only transparent, but the refractive indices of the PDMS and the fluid should be matching as well. In practice the same solution as for PIV was used. Before obtaining good result the phantom must be cleaned. Contamination of old seeding particles at the wall of the Carotid Artery Phantom can cause non-transparency, even though the refractive index is matching. The transmitting and receiving optics are combined in the TSI PowerSight module. The Photodetector Module converts optical signals to electronic signals for the FSA 3500 Signal Processor. Cylinder measurements were performed for this first LDA experiments. Unlike PIV the laser light path is not perpendicular to the phantom wall. Instead, the beams will reach the measurement position by an angle. Therefore the beams are already refracted at the first transition from air to PDMS. When the beam reaches the channel where the fluid is going through, it should not be refracted due to index matching. However, slight imperfections of the index matching will cause refractions of the beam and thus influencing the crossing location of the beams. Due to the gaussian nature of the laser beam the measurement volume has an elliptic form. The cross-section of the cylinder was scanned using a traverse that moved the whole system over the diameter of the cylinder, indicated as a dotted line in figure 3.5. With the velocity vectors in each discrete point a Poiseuille flow profile should appear. About 50 points were measured over a diameter of 16 mm, resulting in a resolution of approximately 0.32 mm. A bandpass filter of 0.1-1 MHz gave the best data rate. The eventual velocity is an average over many detected tracer particles. The amount may be selected manually. Near the wall of the cylinder less tracer particles will cross the measurement volume since the velocity is lower. To keep the measurement time limited the amount of detected particles is decreased.
### Laser Beams

<table>
<thead>
<tr>
<th></th>
<th>Channel 1</th>
<th>Channel 2</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wavelength</td>
<td>561</td>
<td>532</td>
<td>nm</td>
</tr>
<tr>
<td>Focal length</td>
<td>360</td>
<td>360</td>
<td>mm</td>
</tr>
<tr>
<td>Beam Separation</td>
<td>50</td>
<td>50</td>
<td>mm</td>
</tr>
<tr>
<td>Laser Beam Diameter</td>
<td>2.10</td>
<td>2.10</td>
<td>mm</td>
</tr>
<tr>
<td>Fringe Spacing</td>
<td>8.0840</td>
<td>7.6661</td>
<td>µm</td>
</tr>
<tr>
<td>Beam waist</td>
<td>122.45</td>
<td>116.12</td>
<td>µm</td>
</tr>
</tbody>
</table>

Table 3.4: Properties and settings of the laser used for LDA.

### Fluid Properties

<table>
<thead>
<tr>
<th>Substance</th>
<th>Glycerol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density</td>
<td>1180 kg/m³</td>
</tr>
<tr>
<td>Viscosity</td>
<td>(9.25 \times 10^{-3}) Pa · s</td>
</tr>
<tr>
<td>Refractive index</td>
<td>1.4130</td>
</tr>
<tr>
<td>Seeding particle size</td>
<td>8-12 µm</td>
</tr>
</tbody>
</table>

Table 3.5: Properties of the working fluid used for Magnetic Resonance Imaging.

### Resolution

<table>
<thead>
<tr>
<th></th>
<th>PIV</th>
<th>MRI</th>
<th>LDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resolution</td>
<td>0.67 mm</td>
<td>1.25 mm</td>
<td>0.32 mm</td>
</tr>
</tbody>
</table>

Table 3.6: Experimental resolutions obtained for PIV, MRI and LDA.

### 3.6. Resolution

PIV resolution is limited by the pixel sizes and the finite size of the interrogation windows. Interrogation windows are going from 64 x 64 pixels to 16 x 16 pixels with an 50 % overlap, resulting in a final 8 x 8 pixel resolution which equals 0.67 mm. The resolution could be increased by moving the camera closer to the measurement object. The downside is that not the whole object is covered. The optics of the LDA system are able to define a very small measuring volume and thus provides good spatial resolution, typically 100 µm x 1 mm. However, the entire diameter of the cylinder is scanned so that due to time limitation a resolution of approximately 0.32 mm is obtained. The fast signal processing provides excellent temporal resolution. Therefore the temporal resolution is usually limited by the concentration of seeding rather than the measuring equipment itself. MRI data gave 120 pixels in the x-direction which results in a resolution of 1.25 mm.
Figure 3.6: The phantom is shown with different media flowing through. As glycerol flows through the phantom, light is not refracted since the refractive index is matching with the refractive index of the PDMS. Therefore, the contours of the phantom are not visible. In the middle, the refractometer is shown, which can measure the refractive index of the fluid.
Figure 3.7: A. The Left Ventricular Assist Device (LVAD). B. Impression of the flow cycle. In case of steady flow, the aquarium pump is inside the white bucket. In case of pulsatile flow the VAD (right bottom) is connected to the flow cycle. At the left hand side the phantom is situated. C. The driving unit of the VAD. D. The Lavision Imager Intense camera. E. Flow cycle. At the top left the red valve for de-airing. F. The black device allows for shifting the phantom accurately to capture each slice. In this picture, the phantom is rotated over 90 degrees to capture the x-z planes.
Figure 3.8: A. Overview of the MRI-room. The phantom is ready to go into the scanner. Long tubes are going through the wall connecting the rest of the set-up, since metal parts are not allowed inside the MRI-room. B. The phantom lies inside a coil on a napkin to catch possible leakage. C. The water reservoir is outside the MRI-room, since the valves contain metal parts. D. Tubes through a hole in the wall connect the phantom with the rest of the set-up.
Figure 3.9: Schematic of the performed PIV measurements. The bottom, decreasing, increasing and top measurements are performed at certain points in the heart pulse. These points are indicated by D, B, I and T in the graph. A total of 32 sets of measurements have been performed, each consisting of a number of slices of 1 mm that covers the whole plane.
Results

In this chapter the results of all the measurement techniques are presented. First the PIV results for the
cylinder will be shown. Subsequently, the results for the Carotid Artery Bifurcation are shown. Due to the large
amount of data, only a selection of results is shown in this chapter. More results are shown in the appendix.

4.1. PIV Measurements Cylinder

Analytical solutions are available for a flow through a cylinder. Therefore a cylinder is used as a test method.
In figure 4.1 the Poiseuille flow results are shown for two different flow rates. The results are obtained by
averaging all the cross-sectional lines in the middle plane. An analytical solution based on the experimental
maximum velocity is plotted together with the results. An average velocity is determined from this experi-
mental maximum velocity and used to calculate the Reynolds number. The higher peak results in a Reynolds
number of $Re=196$ and the lower peak in $Re=79$. The measured shape of the flow is reasonable, however a bit
shifted. This can be explained because the cylinder was not exactly vertical with respect to the camera.

![Cylinder constant flow $Re=79$ and $Re=196$](image)

Figure 4.1: Poiseuille flow in a cylinder is shown for two different flow rates. The results are obtained by averaging all the cross-sectional
lines in the middle plane. An analytical solution based on the experimental maximum velocity is plotted together with the results. An
average velocity is determined from this experimental maximum velocity and used to calculate the Reynolds number.
The relative error is calculated in the same way as in the reference thesis of G. van der Belt [9]. Two different errors are calculated, $\epsilon_1$ and $\epsilon_2$. The first error $\epsilon_1$ is a measure for the difference in flow rate between the experimental value of the velocity and the analytical value. The second error is a measure for the difference for each radial position, so not only for the total flow rate but also for the shape of the Poiseuille flow. These errors are given by

$$
\epsilon_1 = \left| 1 - \frac{\int_{-R}^{R} \sqrt{(v_e)^2} \, dr}{\int_{-R}^{R} \sqrt{(v_a)^2} \, dr} \right|
$$

(4.1)

and

$$
\epsilon_2 = \frac{\int_{-R}^{R} \sqrt{(v_a - v_e)^2} \, dr}{\int_{-R}^{R} \sqrt{(v_a)^2} \, dr}
$$

(4.2)

where $v_a$ is the analytical velocity and $v_e$ is the experimental velocity. The errors following from figure 4.1 are shown in table 4.1.

<table>
<thead>
<tr>
<th>Errors</th>
<th>$\epsilon_1$ [%]</th>
<th>$\epsilon_2$ [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re = 196</td>
<td>0.89</td>
<td>2.27</td>
</tr>
<tr>
<td>Re = 79</td>
<td>1.10</td>
<td>4.54</td>
</tr>
</tbody>
</table>

Table 4.1: Relative errors for Poiseuille flow. Two different errors are calculated, $\epsilon_1$ and $\epsilon_2$. The first error $\epsilon_1$ is a measure for the difference in flow rate between the experimental value of the velocity and the analytical value. The second error is a measure for the difference for each radial position.

The original settings were an initial interrogation window of 64x64 pixels and a final interrogation window of 16x16 pixels. To check whether these settings were indeed desirable, the same middle plane was post-processed using different initial and final interrogation windows. The results are obtained by averaging all the
4.2. PIV Measurements Carotid Artery Bifurcation

cross-sectional lines in the middle plane and shown in figure 4.2. The smaller the interrogation windows the better spatial resolution, however, if insufficient particles exist within each cell, the correlations can weaken by high frequency noise in the displacement estimates. This high frequency noise is clearly visible in the first three graphs. It can be concluded that the interrogation window size has been too small for these graphs. The last three graphs are very similar and much smoother. As a consequence of these results together with the theory that one interrogation area is typically in the range of 12x12-64x64 pixels, it is concluded that the initial settings are desirable.

4.2. PIV Measurements Carotid Artery Bifurcation

Figure 4.3: Illustration of the slices in the x-y plane. Not all slices are shown here to increase visibility.

The velocities in the Carotid Artery Bifurcation were measured with PIV by 'slicing' the phantom. Some of the slices are shown in figure 4.3 to illustrate the principle. In fact, the phantom is sliced in the x-y planes in 24 slices of 1 mm, just as the thickness of the laser sheet. This has been done in the same way for the x-z planes, wherefore the phantom has been rotated over 90 degrees with reference to the laser sheet and the CCD camera. Since the model is larger in the y-direction and the laser sheet remains the same thickness, the number of slices increased to 39 for the x-z plane. To obtain a 3D velocity profile while only two components were measured, the third velocity component was set to zero. The phantom was reconstructed from the combined slices. An iso-surface of both the phantom reconstructed from the x-y planes and from the x-z planes are shown at the sides of figure 4.4. Already at first sight the x-y iso-surface at the left is much smoother than the x-z iso-surface at the right side. Ideally the two iso-surfaces should be identical, however, most likely due to the imperfections in the phantom, especially in the x-z plane and due to the fact that the scattered light from the seeding particles travels a longer distance to leave the phantom, the quality of the raw PIV images was lower in general. Therefore it was harder to draw a mask, i.e. distinguishing between the phantom region and the surroundings. Moreover, the x-z plane-constructed phantom consists of more planes, which increases the human error.

So an obvious question raised from this observation is whether the results are reliable or not. A fair answer could be found in the y-z planes, perpendicular to the main direction of the fluid. In the same figure as the iso-surfaces three cross-sections are shown for both the phantom reconstructed from the x-y planes and from the x-z planes. The locations are indicated by a black line. Apart from the slight differences in geometry, significant differences in velocity magnitudes were found. Especially at the locations just before the bifurcation and at the narrowed (atherosclerosis) part, the reddish parts in the x-y constructed phantom is hardly seen in the x-z constructed phantom. It seems like that the x-z measurements, which have no velocity contribution in the y-direction, are underestimated. Therefore the hypothesis is that the y-component of the velocity is not negligible.

To get an idea of the magnitude of the y-component of the velocity, some slices are extracted from the plot of the magnitude of the y-component of the velocity and the results are shown in figure 4.5. At the left side the magnitude of the y-component of the velocity is shown for two slices. The first slice goes through the Common Carotid Artery and the narrowed part of the Internal Carotid Artery due to atherosclerosis. The
4. Results

Figure 4.4: The iso-surfaces constructed from the plane are shown at the outskirts of the figure. The phantom constructed from the x-y planes at the left side is clearly smoother than the phantom constructed from the x-z planes at the right side. Three cross-sections are shown where significant differences in velocity magnitudes were found. The velocities are made dimensionless by dividing the measured velocities by the inlet velocities $V_0$ (see subsection Reynolds number). The cross-sections correspond with the following slice numbers: 1. 304 2. 583 3. 720 4. 324 5. 621 6. 761. The cross-sections of the x-z plane are shifted due to a different coordinate system.

second slice goes through the start of the bifurcation and a winding part of the External Carotid Artery. The $y$-component of the velocity is apparently small in the Common Carotid Artery. At the start of the bifurcation and a winding part of the External Carotid Artery instead, the contribution is relatively enormous. In the narrowed part of the Internal Carotid Artery $V_y$ is significant as well. The right side of the figure shows the same cross-sections as figure 4.4, but now a comparison is made with the same cross-sections of the magnitudes of $V_y$. Now the cross-sections are both extracted from the x-y plane constructed phantom. Again the $y$-component of the velocity is significant. Therefore it is concluded that the $y$-component of the velocity is not negligible. Hence, the following results will be all extracted from measurements in the x-y plane.

Figure 4.5: Left: The magnitude of the $y$-component of the velocity is shown here for two slices. Right: The same cross-sections of the magnitudes of the velocity are shown for the x-y plane as in figure 4.4 but now a comparison is made with the same cross-sections of the magnitudes of $V_y$. The velocities are made dimensionless by dividing the measured velocities by the inlet velocities $V_0$ (see subsection Reynolds number). The cross-sections correspond with the following slice numbers: 1. 366 2. 188 from the x-z planes and 3. 304 4. 583 5. 720 from the y-z planes.

In figure 4.6 a comparison is made between CFD data, previous PIV data and PIV data obtained for this thesis. At the left hand side, CFD simulations are shown for two different slices of the Carotid Artery Bifurcation for a constant flow with Reynolds number of 284 and an outflow ratio of ICA/ECA=60/40. The data in the middle
4.3. MRI Measurements Carotid Artery Bifurcation

is the PIV data from a previous thesis [9] with a Reynolds number of 284 and the same outflow ratio. The right column shows the obtained PIV data for this thesis with a Reynolds number of 189. The velocities are made dimensionless by dividing the measured velocities by the inlet velocities. Approximately the same slices are extracted, however, hand-made masks and a different amount of slices causes slight differences. Qualitatively the magnitudes and directions of the velocity are in good agreement. Increases in velocity are observed at the same locations. The difference in Reynolds number could account for slight deviations, although the velocities are made dimensionless. As for the PIV measurements only two velocity components are known and for CFD all three velocity components are known, the z-component in the CFD simulations was left out to make a fair comparison. In reference [9] the importance of the z-component of the velocity has been explored and it was concluded that the z-component of the velocity is negligible compared to the other two velocity components.

Figure 4.7 is comparable with figure 4.6 but now the flow is pulsatile. At the left hand side, CFD simulations are shown for two different slices of the Carotid Artery Bifurcation for Reynolds number up to 512, an outflow ratio of ICA/ECA=50/50 and a Womersley number of 5.2. The data in the middle is the PIV data from a previous thesis [9] with the same Reynolds number and outflow ratio. The right column shows the obtained PIV data for this thesis with a Reynolds number up to 189 and Womersley number 5.8. The VAD pumps the glycerol with a sinusoidal flow rate. The flow is measured at approximately the highest point in the cycle, which is shown in the graphs. Compared with the previous figure, less agreement is found. This is probably due to two major causes. Firstly, the relatively large difference in Reynolds number alters the flow profile. Even back-flow is observed in the lowest part of the pump cycle, likely due to the low Reynolds regime. Secondly, the timing of the measurements could deviate. This is nicely illustrated in reference [9] where delays of only 10 ms in the simulations showed big differences in flow profiles. Inaccuracy in the triggering system and instability of the pump cycle can make the exact timing very difficult and therefore the experimental flow profiles deviate.

4.3. MRI Measurements Carotid Artery Bifurcation

MRI measurements were performed with water instead of glycerol since the hypothesis was that water will give a better contrast relative to glycerol. It is hard to say something about this property because contrast was added to the water to be ensured of a sufficient signal. Since the viscosity of water is a factor ten lower than the viscosity of glycerol and the density is only a factor 1.1 - 1.2 lower, the velocity of the fluid had to be decreased. Actually the velocity had to be in the order of 1 - 3.5 cm/s, however, it turned out to be very hard to achieve such low velocities, firstly because the magnetic flow meters were not designed to measure such low flow rates and secondly because the pump had a minimum flow setting which was much higher. Friction could also not lower the flow rate sufficiently, despite the long tubing. So the flow had to be suppressed with the help of clamps. For this reason it was decided to measure only constant flow with relatively high Reynolds numbers, Re≈ 500. The flow rate was not read out from the flow meters anymore but was obtained from the MRI software, just as the outflow ratio. Two full measurements were done by around 22° C. The first measurement had an outflow ratio of ICA/ECA=50/50 and the second had an outflow ratio of ICA/ECA=60/40. The flow cycle was free of air bubbles because soap was added to the water. The results for two slices and the two outflow ratios are presented in figure 4.8 and 4.9 together with results from previous measurements [9]. A hand-made mask is made from CFD slices. The mask is used to select the geometry from a large 3D matrix containing velocity vectors. Firstly, it strikes that the results are much smoother than the reference images. The reason could be that air bubbles were present in the reference measurements and that the signal was weaker because no contrast was added. Qualitatively, however, the reference images in the ICA/ECA=60/40 case show better agreement with the PIV and CFD images, since the MRI results do not even show reddish velocity increasing in the narrowed parts. The results with an outflow ratio of ICA/ECA=50/50 are much more promising. Qualitatively the results show good agreement with the PIV results, except for the narrowed part in the upper image. It should be noticed though that the Reynolds numbers differ significantly which makes a comparison questionable.
4. Results

Figure 4.6: At the left hand side, CFD simulations are shown for two different slices of the Carotid Artery Bifurcation for Reynolds number 284 and an outflow ratio of ICA/ECA=60/40. The data in the middle is the PIV data from a previous thesis [9] with a Reynolds number of 284 and the same outflow ratio. The right column shows the obtained PIV data for this thesis with a Reynolds number of 189. The data in the middle and right column is from different slices, however, small differences are expected. Approximately the same slices are extracted, however, hand-made masks and a different amount of slices cause slight differences.
4.3. MRI Measurements Carotid Artery Bifurcation

Figure 4.7: At the left hand side, CFD simulations are shown for two different slices of the Carotid Artery Bifurcation for Reynolds number up to 512, an outflow ratio of ICA/ECA=50/50 and a Womersley number of 5.2. The data in the middle is the PIV data from a previous thesis [9] with the same Reynolds number and outflow ratio. The right column shows the obtained PIV data for this thesis with a Reynolds number up to 189 and Womersley number 5.8. The velocities are made dimensionless by dividing the measured velocities by the inlet velocities. Approximately the same slices are extracted, however, hand-made masks and a different amount of slices causes slight differences.
4. Results

Figure 4.8: PC-MRI results are shown for two different slices and compared with previous measurements [9]. (a) is obtained with a 7 T MRI scanner using an aqueous glycerol solution. (b) is obtained for this thesis with a 3 T MRI scanner using water with soap and contrast. A hand-made mask is made from CFD slices. The mask is used to select the geometry from a large 3D matrix containing velocity vectors. (a) Previous results with an outflow ratio of ICA/ECA=60/40 and a Reynolds number of $Re=284$. (b) Obtained MRI results with an outflow ratio of ICA/ECA=60/40 and a Reynolds number of $Re=500$.

Figure 4.9: PC-MRI results are shown for two different slices and compared with previous measurements [9]. (a) is obtained with a 7 T MRI scanner using an aqueous glycerol solution. (b) is obtained for this thesis with a 3 T MRI scanner using water with soap and contrast. A hand-made mask is made from CFD slices. The mask is used to select the geometry from a large 3D matrix containing velocity vectors. (a) Previous results with an outflow ratio of ICA/ECA=50/50 and a Reynolds number of $Re=284$. (b) Obtained MRI results with an outflow ratio of ICA/ECA=50/50 and a Reynolds number of $Re=500$. 
4.4. LDA Measurements Cylinder

Two LDA measurements have been performed in a cylinder with a Reynolds number of 160 using a glycerol solution with tracer particles. The results are shown in figure 4.10 together with the analytical Poiseuille flow in a cylinder. The velocities are averages over multiple counts of tracer particles that pass the measurement volume. In general the results of both measurements show good agreement with the analytical solution. However, some results deviate strongly from the analytical solution. One of these points is indicated with a square and marked as 'c' in figure 4.10. To understand why the velocity is much lower than expected, the histograms of some neighbouring points are studied. These points are indicated as 'a', 'b', and 'd' in figure 4.10 and the histograms of these four subsequent points are shown in figure 4.11. The histogram of point c has smaller velocities than expected from the analytical solution. It is not likely that this is just a measurement error since all these histograms are constructed from 10000 counts, i.e. the velocity of 10000 tracer particles was consequently estimated too low. A possible explanation could be that the LDA system had not stabilized after the movement to the next position. Stabilization was in particular a problem when turning on the LDA device. Another possibility is that due to slight imperfections in the PDMS casting and/or in the index matching the laser beams were not in the same way refracted and therefore crossed in a different location or did not cross sufficiently at all. To investigate the hypothesis that the location is influencing the measurements and not a time-dependent factor such as stability of the laser, the velocity measurement is repeated 11 times in one point. The means and variances are shown in table 4.2. Although the velocities do not deviate so much as the velocity in point c does, the difference between the highest and lowest value is significant. The deviations is for both around 11% of the mean value of the mean values. The strong deviation of point c is potentially due to a combination of the location and the reliability of the measurements. It should be mentioned that some measurement points from figure 4.10 were repeated if they seemed to be wrong. Moreover, complete sets of measurements are not shown in the results because at some point the LDA system gave velocities which were too low and the spread in the histogram was very large. Another frequently seen phenomena is that the histogram showed two peaks; one around zero and one around the value it should be. Additionally, LDA measurements are time consuming compared with PIV or MRI. If a full 3D image of the Carotid Artery Bifurcation is made, the effort is disproportionate. However, LDA is a very appropriate measuring technique for a small volume, for example the narrowed part in the Carotid Artery.

Figure 4.10: LDA velocity measurements in the vertical cross section of a cylinder. Measurements 1 and 2 are independent. The velocities are averages over multiple counts. The solid line is the analytical solution for the Poiseuille flow for Reynolds number 160. The histograms of the subsequent measurement a, b, c and d are shown in figure 4.11. Point c clearly deviates from what is expected from the analytical solution.
Figure 4.11: The histograms of the measurement points a, b, c and d from figure 4.10. The histogram of point c has smaller velocities than expected from the analytical solution.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Mean</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0303</td>
<td>0.0109</td>
</tr>
<tr>
<td>2</td>
<td>0.0335</td>
<td>0.0104</td>
</tr>
<tr>
<td>3</td>
<td>0.0270</td>
<td>0.0106</td>
</tr>
<tr>
<td>4</td>
<td>0.0347</td>
<td>0.0102</td>
</tr>
<tr>
<td>5</td>
<td>0.0327</td>
<td>0.0103</td>
</tr>
<tr>
<td>6</td>
<td>0.0315</td>
<td>0.0105</td>
</tr>
<tr>
<td>7</td>
<td>0.0339</td>
<td>0.0104</td>
</tr>
<tr>
<td>8</td>
<td>0.0284</td>
<td>0.0106</td>
</tr>
<tr>
<td>9</td>
<td>0.0320</td>
<td>0.0102</td>
</tr>
<tr>
<td>10</td>
<td>0.0325</td>
<td>0.0106</td>
</tr>
</tbody>
</table>
| 11          | 0.0273| 0.0101             | **0.0313**

Table 4.2: LDA measurements in one point are repeated. For each measurement 10000 tracer particles were counted. In figure 4.10 the first mean value is used. At the bottom of the column the mean value of the mean values is shown.
5.1. Conclusion

1. Are PIV measurements in the Carotid Artery Bifurcation reproducible?

The PIV results in the Carotid Artery Bifurcation show indeed similar results. Qualitatively the flow is in magnitude and direction very similar. Therefore the reproducibility of the PIV measurements is demonstrated. A number of parameters in the measurements and in the post-processing could result in slight deviations. It is hard to get exactly the same Reynolds number because the flow meters register what should be a constant flow as a fluctuating flow of +/- 0.1 L/min. This corresponds to a deviation of the Reynolds number of +/- 17. Moreover, the valves in the flow cycle are very hard to adjust accurately. Impurities in the PDMS and seeding particles that stick to the interior account for blurry spots in the PIV measurements. Especially in the x-z measurements the effects were visible. As the model becomes older, this problem will only increase. Also, the first slice is chosen by human eye. Therefore the first slice will alter each measurement and consequently all slices will differ slightly in position. It is therefore difficult to compare exactly the same slice. The error would be in the order of 0.1-0.5 mm.

2. Can the third dimension be added to the PIV measurements by measuring a perpendicular plane to obtain a third velocity component?

It has been taken into consideration to add the z-component of the velocity measured in the x-z plane to the x-y plane measurements to have the velocity vectors in all directions. However, for the x-y plane measurements only 24 z-planes or ‘slices’ of 1 mm are measured. As a consequence, only 24 z-velocity vector components can be added for each x-y pair. Therefore the z-velocity vector components must be discretized and averaged. In other words, the same value should be given to all the y-positions within one slice. Similarly, only 39 x-z planes are measured and therefore only 39 different y-planes are available to match a z-velocity component. The y-component in the x-y measurements must be discretized by dividing the y-axis into 39 parts. Due to these interpolations the error would become too large. Therefore it is decided that the measurements are not combined but showed separately. From the results it is concluded that the y-component of the velocity is not negligible and should therefore not be set to zero if only the x- and z-components of the velocity are measured. It is also concluded that too much information is thrown away by combining the two measurements. Moreover, the z-component of the velocity turned out to be much smaller than the x- and y-component. Consequently, measuring in the x-z plane does not provide sufficient information relative to the effort.

3. Could MRI results be improved?

MRI measurements were performed with water instead of glycerol since the hypothesis was that water will give a better contrast relative to glycerol. It is hard to say something about this property because contrast was added to the water to be ensured of a sufficient signal. The smoothness of the images has certainly improved. Air bubbles were absent due to soap. Qualitatively the results mostly show good agreement with the PIV results. A drawback though is that the Reynolds numbers differ significantly which makes a comparison questionable.
4. Is Laser Doppler Anemometry a suitable measuring technique to measure the flow in the Carotid Artery Bifurcation model?

In general the LDA results show good agreement with the analytical solution. The technique can provide high resolution velocity information. It applies to LDA that the high resolution is at the cost of time. Therefore LDA is suitable to accurately measure only the high-interest parts of the Carotid Artery, for example the narrowed part in the Internal Carotid Artery. Some results deviate strongly from the analytical solution. A possible explanation could be that the LDA system had not stabilized after the movement to the next position. Another possibility is that due to slight imperfections in the PDMS casting and/or in the index matching the laser beams were not in the same way refracted and therefore crossed in a different location or did not cross sufficiently at all.

5.2. Discussion

- The flow meters register what should be a constant flow as a fluctuating flow of +/- 0.1 L/min. This corresponds to a deviation the Reynolds number of +/- 17. A precise Reynolds number could therefore not be obtained. The average Reynolds number should however be around those values.

- For comparing pulsatile PIV measurements with CFD, it is almost impossible to capture the same moment in the pulse. It has been shown [9] that after 10 ms a big difference in flow profiles can appear.

- The flow meters indirectly trigger the laser for PIV. For pulsatile flow however, the periods are not exactly identical and therefore the laser is triggered not exactly at the same moment in the pulse.

- LDA measurements should take place in the beam waist to get optimal performance from any LDA equipment. Since measurements are done in a cylinder, particles are flowing not only through the beam waist. So particles outside the desired beam waist could influence the measurements negatively.

- During LDA measurements, large fluctuations of the data rate were observed, i.e. large fluctuations of the amount of detected seeding particles per unit time.

- The LDA solution was contaminated. Unlike for PIV, for which this is natural seeding, the LDA measurements could be distorted.

- The middle of the cylinder is found by eye now. Due to the relatively large measuring volume, i.e. the crossing of the beams, it could be that the line over which has been measured is not exactly the diameter of the cylinder.

- A larger number of points could have been measured for LDA, however, the measuring time would have increased while the obtained resolution seemed sufficient.

5.3. Recommendations

- Use a smaller particle size for LDA. For the experiments particle sizes of 8-12 µm were used, while typical seeding particles are 1 µm.

- Investigate the influence of the refractive index matching on LDA results.

- Clean the solution from natural seeding for LDA to prevent background noise.

- The measurement points for LDA were now 0.32 mm apart. Since the traverse can move very accurately, the number of measurement points can be increased.

- Calibration for PIV was difficult. One could either choose to let Davis convert the data to m/s. It is also possible to go from pixels and the chosen delta t to m/s by hand, using a conversion factor obtained by a ruler.

- It is difficult to measure small velocities in MRI scanner, the best option will be probably glycerol with contrast. A stronger pump is necessary in that case.
Appendix
Figure 6.1: At the left hand side, CFD simulations are shown for two different slices of the Carotid Artery Bifurcation for Reynolds number 284 and an outflow ratio ICA/ECA=50/50. The data in the middle is the PIV data from a previous thesis \[9\] with a Reynolds number of 284 and the same outflow ratio. The right column shows the obtained PIV data for this thesis with a Reynolds number of 189 (Slice number 90 and 147). The data in the middle is approximately the same data, however, hand-made masks and a different amount of slices cause slight differences.

\[
V = \frac{V_m}{V_0}
\]
Figure 6.2: The left and right column show the obtained PIV data for three different slices (number 67, 107 and 142) of the Carotid Artery Bifurcation for Reynolds number 82 and 189, respectively, and an outflow ratio of ICA/ECA=50/50. The velocities are made dimensionless by dividing the measured velocities by the inlet velocities, \( V = \frac{V_m}{V_0} \). The data show very similar qualitative results for the two Reynolds numbers. This is what can be expected, since both Reynolds numbers are in the laminar regime. Approximately the same slices are extracted, however, hand-made masks and a different amount of slices causes slight differences.
Figure 6.3: The left and right column show the obtained PIV data for three different slices (number 67, 107 and 142) of the Carotid Artery Bifurcation for Reynolds number 82 and 189, respectively, and an outflow ratio of ICA/ECA=60/40. The velocities are made dimensionless by dividing the measured velocities by the inlet velocities, \( V = V_m/V_0 \). The data show very similar qualitative results for the two Reynolds numbers. This is what can be expected, since both Reynolds numbers are in the laminar regime. Note that the dimensionless velocities are slightly lower than the dimensionless velocities in 6.2. Since the 60/40 outflow ratio is considered to be more natural [26], the fluid is less forced to flow through the ECA than for the 50/50 ratio and hence, the dimensionless velocities are lower.
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