IN VITRO EVALUATION OF THE INFLUENCE OF A BILEAFLET MECHANICAL AORTIC VALVE ON CORONARY FLOW

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1. Introduction and Motivations

The cardiovascular system provides for the transport of blood to any part of the human body. Its role is to provide every cell with nutriments and oxygen, removing carbon dioxide and other metabolic wastes from it. Blood also takes part in thermoregulation processes and works as a carrier for chemical signals. More in general we can say that the blood circulation provides for the “homeostasis” of body cells.

1.1 The coronary arteries

The heart itself, as a living tissue, needs nourishments, which reach the heart cells by particular vessels called coronary arteries. These arteries arise from the first part of the ascending aorta, in a region called sinuses of Valsalva. The right coronary artery (RCA) normally supplies the posterior side of the heart. The left coronary artery divides in the left anterior descending artery (LAD) and the in the circumflex artery (CX). The LAD supplies the front part of the heart, the CX the lateral side and the posterior side (see fig 1.1).

Figure 1.1: Anatomy of the coronary arteries. Notice the different branches of the coronary arteries providing different part of the heart with blood. Differences in anatomy among subjects are seen.
When the coronary arteries are not able to provide the right amount of blood flow, the heart is forced to work out of his physiological conditions. This will result in a shortage of oxygen and nourishments. This situation in which the heart cells do not receive enough oxygen is called ischemia and this often causes chest pain. This shortage of oxygen may result in an infraction if reperfusion is not established in time. If a very low perfusion involves a wide part of tissue, the entire contractive function of the heart can be compromised. Therefore it is important to ensure a right, physiological coronary flow.

Coronary flow is not a simple issue. Like in other arteries, coronary flow depends on the pressure of the vessel from which they arise and on the resistance the vessel itself opposes. This resistance, like in other blood vessels, can be changed by the contraction of muscular cells in the vascular wall major difference between the coronary arteries and other blood vessels.

Unlike the other blood vessels, coronary arteries are directly affected by the pressure of heart walls itself. The heart tissue, contracting around coronary arteries, squeezes them thereby reducing coronary inflow, enhancing outflow and increasing the resistance and as a consequence limits the blood flow in systole. This explains why coronary flow raises during diastole, when heart walls are relaxed, fig. 1.2.

The role of the aortic pressure is to overcome these resistances and make perfusion possible. In other words aortic pressure represents the energy used to establish the flow. Some experiments [1] showed how an increase in aortic pressure directly leads to a raise in coronary flow. Therefore, we can take aortic pressure as one of the main parameters for coronary perfusion. On the other hand, some studies [2] suggest that the hemodynamic situation in the aortic root influences coronary perfusion.

In particular, velocities in aorta might play a role in the coronary perfusion. The study of R.E. Hayes in 1989 [16]focused on the effect of the Reynolds number in a pipe on the flow in a 90 degree planar branch. The study was carried out with the CFD (computational fluid dynamic) method in steady laminar flow conditions, (see fig 1.3). Although our experiments series on
coronary flow mainly focused on pulsatile flow, this study gives an evidence, in simplified conditions, of the influence of the velocity on the flow in side branches (in our case, the coronary arteries).

Figure 1.3. Dominium geometry, coordinate system and boundary conditions in the finite element study by R. E. Hayes

The Reynolds number can be written as:

\[ Re = \frac{\rho V D}{\mu} \]

Where, \( \rho \) in the fluid density, \( V \) is the mean velocity in the conduit, \( D \) is the characteristic length (equal to diameter if the cross section is circular), \( \mu \) is the fluid viscosity.

Therefore keeping unchanged the geometry (and of course the fluid) increasing the Reynolds number means increasing the velocity.

The study of R.E. Hayes [16] showed recirculation zones at the entrance of the side branch for increasing Reynolds number (Re) values. See picture below.
Figure 1.4: Streamline contours for the case of equal exit pressures (P in figure 1.3) in the two branches. For increased Re a recirculation zone develops at the enter of the branch. The recirculation decreases the flow in the side conduit. The ratio between the flow in the main conduit and the side branch for increasing Reynolds number and different size of the side branch has been described in the graph in figure 1.5.

Figure 1.5: Effect of increasing Reynolds number on the flow split for various side branch widths. Ds indicates the ratio between the diameter of the side branch and the radius of the main conduit. It can be seen that for increasing Reynolds number the flow in the side branch decreases. Therefore, increasing the velocity of the fluid in pipe causes recirculation which disturbs the flow in the side branch. On the other hand it has also to be noticed that with decreasing diameters of side branches this effect is less remarkable. Hence the effect of the geometry is important to determine whether the effect of the velocity on is more or less pronounced in our conduit.
1.2 The aortic valve and Fluid Dynamics in the proximal aorta

The aortic valve consists of three cusps, or leaflets. The leaflets are attached to the first part of the proximal aorta forming the annular ring that separates the aorta from the left ventricle. Behind the leaflets three cavities are present, called sinuses of Valsalva. The sinuses represent a “dilatation” of the base of the aorta and appear as three bulges in the aortic root, see fig. 1.6.

![Diagram of aortic valve and sinuses](image)

Figure 1.6: Position of the Sinuses of Valsalva in aortic root (left), and 3D reconstruction of the sinuses (right), with permission of Jurgen de Hart, Fluid-Structure Interaction in the Aortic Heart Valve, 2002.

The coronary arteries arise from two of these sinuses. Therefore the leaflets facing the coronary arteries sinuses are called “left / right coronary cusps” and “non coronary cusp” the remaining one. The aortic valve is designed to allow blood to flow in one direction from left ventricle to the aorta. The aortic valve opens at the beginning of systole when the left ventricle contracts and pushes the blood into the aorta. The valve closes before the start of diastole during which the ventricle relaxes and fills from the atrium. In resting conditions systole lasts about one third of the cardiac cycle. During ejection, blood rapidly accelerates through the valve and reaches a peak velocity after the leaflets are fully opened. Peak flow (Pf in fig. 1.7) is reached during the first third of systole and then the flow starts to decelerate. The valve closes at the end of deceleration phase with very little reverse flow. Figure 1.4 shows a typical flow pattern for pressure and flow in aorta during cardiac cycle.
In the late part of systole vortices form in the sinuses of Valsalva. These vortices usually originate in a region between the edge of the cusps and the aorta wall. Vortices usually start after the peak of systole (Ps in fig 1.7) when the gradient of pressure inverts and a deceleration in blood flow occurs. During the second part of systole the center of these vortex moves towards the centre of sinuses, and last until the end of the systole. This mechanism is at the base for the correct closure time and motion of a native valve. A healthy valve does not show any significant reverse flow (also called closing volume) because the cusps close softly, before the flow inverts. The absence of the sinuses of Valsalva results in irregular and delayed closure of the valve [3]. The back flow amount in this case can reach 25% of the ejected volume of blood. Therefore, without the sinuses of Valsalva also a native valve needs a reverse flow to close. On the contrary, in normal conditions, a native valve closure is guided from the pressure gradient mechanism rather than the back-flow effect.
1.3 **Aortic valve diseases and their influence on the heart**

In valve diseases the aortic valve presents abnormalities or malformations that prevent its normal functioning. The origin of the valve diseases can be congenital or due to acquired pathologies. Heart valve diseases are closely related to heart pathologies, since malfunction of the valve directly results in a loss of efficiency of the pumping of the heart. Diseased aortic valves present themselves as being stenotic, insufficient or both.

### 1.3.1 Aortic valve stenosis

The most common cause of aortic stenosis is the degenerative calcification of the leaflets. Calcium deposits on the leaflets progressively cause the fusion of the leaflets and increase their stiffness. A stenotic valve results in a narrowing which obstructs blood which flows during systole and causes a pressure gradient between the left ventricle and the aorta. The heart has to overcome this extra gradient to establish the normal perfusion and this is achieved by increasing the ventricular pressure during systole. The heart typically responds to this further load by increasing the thickness of its muscular tissues in order to provide for stronger contractions. Due to this increased strength in contraction additional squeezing of the coronary vessels during systole occurs, which represents a non physiological condition. It can be observed that in case of severe aortic stenosis back flow in coronary arteries is present during systole as a result of this increased intramyocardial pressure. As a result less blood reaches the heart cells and may even cause ischemia due to the increase demand but decreased supply. Therefore stenotic valves represent a risk for coronary perfusion and, more in general, for the healthy condition of the heart.

### 1.3.2 Aortic valve insufficiency

The majority of aortic insufficiency occurs due to rheumatic heart disease. Post inflammatory diseases of rheumatic origin progressively destroy the cusps of the aortic valve. Therefore the correct and complete closing of the valve is hampered. The incomplete closure allows backflow into the left ventricle reducing the net forward flow. The heart usually responds to this extra volume load by increasing the size of the left ventricle cavity and by doing this increasing the stroke volume in order to maintain the normal cardiac output. This response tends to normalize strains along the muscle fibers of the heart. Dimension of the heart can become too large to allow the cardiac fibers to establish the needed ventricular pressure and heart failure can be the result.

Resuming an aortic stenosis causes an extra pressure load for the heart; insufficiency, causes an extra volume load for the heart. Normally it is possible to live with a stenotic /insufficient valve. However, when these diseases become severe and valve function is seriously compromised, valve replacement becomes necessary.
1.4 Prosthetic aortic valves

Valvular heart disease afflicts millions of people worldwide and leads to 250,000 valve repairs or replacements each year [4]. Approximately 180,000 prosthetic valves are implanted each year throughout the world. Mechanical heart valves (MHV) are devices built to replace the diseased natural valves. However, the MHVs are not bio-morphed, they are not designed to mimic the shape of a native valve. All the MHVs are based on a occluding structure that moves during the cardiac cycle allowing the flow only in one direction. The design of the occluding structure differentiates the various types of MHVs: caged ball, tilting disk and bileaflet valve. The most commonly used bileaflet valve, the St Jude Medical mechanical valve (SJM), has two semicircular leaflets that drives the forward flow through three regions; two major orifices and a central orifice. The major part of the flow runs through the major orifices. The jet pattern shown in fig. 1.8 characterizes the forward flow.

![Figure 1.8: Flow patterns downstream a bileaflet MHV (Fluid Mechanics of Heart Valves Annu. Rev. Biomed. Eng. 2004. 6:331-62). On the axis on the side velocities in cm/s have been computed at peak systole.](image)

The aim of MHVs is to replicate the function of a native valve even with different design characteristics. Opening is a reasonably easy achievable mechanism. During contraction the pressure in the left ventricle overcomes the pressure in aorta and the natural leaflets open allowing the flow without any additional resistance. Prosthetic leaflets of a MHV open following the same principle, and the opening movement does not require a large amount of energy. Although the leaflets can open easily the valve itself introduces a narrowing in the outflow.. The sewing ring, necessary to implant the valve, reduces the original area of flow. Therefore the valve represents an obstruction during systole. The pressure gradient, resulting from this obstruction can be measured directly in experimental set-ups or indirectly, with Doppler ultrasound in vivo[8,11]. The closure mechanism of the heart valve is not equally easily achievable as opening mechanism. Healthy aortic valves close without back flow. Indeed they close before the flow inverts its direction. MHVs cannot replicate this behavior because of their design. Normally a MHV closes because of back flow, that, depending on the valve (size and design), can be up to 20% of the ejected volume [4].
From the foregoing reasons we can infer that the hemodynamic situation in the proximal aorta is dramatically changed by any MHV both for systole and diastole. Figure 1.9 shows the different flow patterns for a native valve (a) and a mechanical bileaflet valve (b).

A question is to understand if these changes in flow (pressure and velocities) in the aortic root can really affect coronary flow. If coronary perfusion mainly depends on aortic pressure then our analysis should focus on the pressure distribution on proximal aorta. Pressure drops in this region could be ascribed to the expected pressure gradient induced by the valve as mentioned before. Another reason for the pressure drop might occur as a result of the Venturi effect. The Venturi effect can be seen in pipes when a reduction of diameter occurs. The result is that in the those region the pressure drops. The explanation of the phenomenon starts from the conservation of mass, which yields the conservation of flow (Q) for two sections of a rigid pipe. The flow entering the pipe in figure 1.10 at A has to be the same as the flow through the area A2.

Then:

\[ V_1 * A_1 = V_2 * A_2 \]  \hspace{1cm} (1.1)

Therefore if the section area decreases, the velocity has to increase of the same ratio in order to verify the conservation of flow equation (1.1).

In the case of steady flow if we assume that the energy loss for viscosity is neglectable the energy is then divided between pressure and velocity. Hence if we assume there is no dissipation along the conduit and the energy is conserved, we can state that the energy amount will be the same for two sections of this conduit (A1 and A2 in figure 1.10).

That yields to Bernoulli equation [17]:

\[ P_1 + \frac{1}{2} \rho V_1^2 = P_2 + \frac{1}{2} \rho V_2^2 \]  \hspace{1cm} (1.2)

If the area in section A2 is smaller than the area in section A1, the velocity in section A2 has to be higher than in section A1, according to eq. 1.1. Subsequently the pressure in A1 has to be higher than the pressure in A2 in order to satisfy eq. 1.2. It is called “The Venturi effect” the loss in pressure drop in A2 with respect to A2 and it can be resumed as in fig 1.9:
Therefore we can expect an additional pressure drop due to this effect that sums to the pressure gradient induced by the obstruction of the valve. If the total amount of the pressure drop becomes remarkable we might find that the pressure in aorta is not sufficient to establish the normal coronary perfusion. However, other parameters may play a role in coronary perfusion. Even assuming that the pressure in aorta is not remarkably changed by the presence of the valve we cannot neglect the fact that the velocity patterns are dramatically modified. In fact changes in coronary flow might be also due to these altered velocity patterns, characterized by two jets in which the velocities can be much higher than the normal. (See fig 1.9). It is not completely clear whether coronary flow is affected the velocity distribution at the ostium. Moreover, the absence of the cusps might result in abnormal formation of vortices or even absence of the vortices and subsequently the effect on coronary flow has not been fully clarified.

So in summary the presence of the valve can indeed affect the normal coronary perfusion in different ways but the real effect of each factor has been not completely explained yet.
1.5 Valve orientation in vivo

Surgeons implant the valve slightly in the left ventricle (sub annular) or towards the aortic root (supra annular) depending on the anatomy of each patient. The shape of the aorta determines the modality of implant. During the surgery one of the aims is to achieve the best matching between the orifice obtained by removing the diseased valve and the sewing ring of the prosthetic valve.

The optimum orientation of a prosthetic aortic valve is still an open question. Nowadays, this decision is mainly left to the surgeon’s own experience and background. Flow in the aorta during systole is not symmetric across the section. It is possible to detect an area of major flow, near the non coronary cusp, in which higher velocities occur. Leaflets in the case of a bi-leaflet valve can meet this area in different ways, depending on the position of the leaflets. The leaflets can be placed with one of the hinges toward the non coronary cusps (A orientation in figure 1.8) or 90 degrees rotated, with the hinges facing the RCA and LCA respectively (B orientation in figure 1.10).

![A orientation and B orientation](image)

*Figure 1.10: Position of the leaflets with respect of the area of major flow in aorta and with respect to the coronary arteries for a bi-leaflet valve. In A orientation the leaflets cross the major flow area, in B orientation the area of major flow matches with one of the valve main orifices.*

Besides the issues mentioned in paragraph 1.4 the orientation of the valve can influence other aspects of hemodynamics. First we consider the resistance to the flow. We can imagine that leaflets in orientation A represent a bigger obstruction to the flow than in orientation B. This could lead to a higher pressure gradient induced by the valve. Secondly we consider the issue of hemolysis. The high velocities of the blood flow along the leaflets of the valve result in high shear forces on the red blood cells. This might destroy the red blood cells.

Thirdly, coronary flow changes as a result of the valve orientation, according to Kleine at al. [10]. These studies, however, do not give a complete description and analysis of the phenomena involved in this problem.

On the other hand in vitro studies or computational fluid dynamics (CFD) analysis focuses mainly on the flow downstream a bileaflet valve, or on the opening/closing mechanics of the valve [4,9]. However the link still misses between the information that these studies provide on the fluid dynamic situation in the aortic root and the possible effect on coronary circulation. The difficulties on linking the fluid dynamic situation in the aortic root and the possible influence
on the coronary perfusion lie in the limitation of both the experimental and the in-vivo models and numerical model. The human body cannot be replicated or modeled in its every aspect.

Modeling means reducing complexity making assumptions or simplifications in order to study some particular features of a more complex phenomenon. Therefore, the result achieved cannot be applied directly to the human in vivo situation, which involves all the physiological or pathological parameters without any restriction.

On the other hand in vivo studies allow measuring the parameters of interest in the real condition. In vivo studies, however, can only offer a partial physical explanation of the results suggesting possible causes of the phenomenon without investigating them.

In 2002 Kleine et al. published the paper “Effect of mechanical aortic valve orientation on coronary artery flow: Comparison of tilting disk versus bileaflet prostheses in pigs”.[10] This work investigates the influence of valve orientation on coronary blood flow.

In the result part of this article the bileaflet valve showed a difference in LAD flow between orientations A and B (see also figure 1.8). With a cardiac output of 4.3 l/min the average flow in orientation A was 46 +/- 9.7 ml/min versus 34 +/- 9.4 ml/min in B. With a cardiac output of 5.9 l/min the flow average in orientation A was 77 +/- 8.8 ml/min versus 62 +/- 5.3 ml/min in B. Unfortunately, no information is given with respect to the flow patterns during the cardiac cycle. Therefore it is not possible to understand whether differences mainly occurred in systole, diastole or in both. It is not clear if the orientation of the valve can indeed affect coronary flow also in diastole as a consequence of changes in flow patterns in the aortic root or due to the closure mechanics of the valve. Moreover no fluid dynamic explanation of these changes has been given. It has been suggested that turbulence that forms starting from the hinges can disturb coronary flow. Possible reasons of this disturbed flow due to turbulence are not well known. Furthermore, turbulent flow (according to the author) appears 4 cm downstream from the valve, while coronary arteries arises in a range between 1 and 1.5 cm downstream the valve.

Another limitation of the study is that the flow rates obtained are no comparable with the flow obtained preoperatively. Flow rates before the implantation were in the range of 25.0 +/-3.4 ml/min so after the operation flow rates were almost doubled. This is most likely due to the effect of the medication and of cardioplegic treatment that dilates the coronary vessels and reduces their resistance, increasing the blood flow. Therefore it is not possible to state whether the presence of the valve itself, regardless of the orientation, can affect the coronary flow. Another important point of the investigation refers to the increasing of the cardiac output. In the study cardiac output was increased from 4.3 to5.9 l/min. This raise in cardiac output (14 %) led to a decrease in the difference between the two positions. Differences in flow rates went from 26% for 4.3l/min cardiac output to 19% for 5.9 l/min cardiac output. This decreasing in the differences for higher cardiac output has not been explained. Possible reasons can be due to the turbulence phenomena that take place with higher flow rates. Since in turbulence fluid layers cannot be distinctly recognized the effect of the orientation might be reduced.

The coronary flow during the cardiac cycles is of major importance. As mentioned in paragraph 1.1 the resistance of the coronary arterioles can change. During maximum exercise the muscular sphincters surrounding the arterioles are relaxed, opposing a minimal resistance to the blood flow. If the maximal coronary flow is hampered by any cause, complaints as shortness of breath or chest pain can occur. Even though influence of different orientation of prosthetic valve on coronary blood flow is shown in Kleine’s article [10] for increased cardiac output, the question remains for maximal achievable coronary flow.
1.6 Aim of the study

The aim of the study is to investigate the effect of the valve orientation on coronary flow with in vitro experiments. In particular the aim is to determine whether by changing the orientation of the prosthetic aortic valve it is possible to measure an increase or decrease in coronary flow. The study is divided in two series of experiments: Experiments on flow and experiments on pressure. The experiments on coronary flow are performed to compare the in vitro results with the results obtained in vivo by Kleine et al [10]. The experiments on pressure are performed to investigate if pressure is altered by the orientation of the valve and as a result the flow is influenced. The purpose of this approach is to combine the results coming from the two series to be able to explain which are the parameters important for coronary perfusion and whether the measure of them can be acquired in vivo with the same instruments. Moreover, the experimental set up allows performing measurements in more controlled conditions and, in addition, permits methods and devices that cannot be used in vivo since they would represent a too invasive procedure.
2. Description of the set-up

2.1 Steady flow set-up

The steady flow set up consists of a system of a barrel and a reservoir (respectively B and RES in fig. 2.1) placed at different heights and connected by a pipe made in polyurethane (the aorta). The circuit is filled with water. The water flows from the barrel placed above through the aorta towards the reservoir. The flow rate from the barrel to the reservoir is controlled by a resistance (Rao in fig 2.1) placed downstream the aorta. The barrel is refilled with water by a pump (P in fig. 2.1), that drives the flow from the reservoir to the barrel. The valve is placed upstream the aorta as will be explained later.

![Figure 2.1: Steady flow set-up model.](image)

The water flows through the aorta from the barrel B, placed higher, to the reservoir RES. Rao is an adjustable resistance placed downstream the aorta and allows changing the flow rate in the aorta. The pump P drives the water from the reservoir to the barrel, closing the circuit. The valve is inserted upstream the aorta.
2.2 Pulsatile flow setup

The pulsatile flow set up consists of a system of chambers and pipes filled with water. The scheme of the model is given in figure 2.2. A 40 cm long straight tube made from polyurethane represents the aorta in the vitro model. A left ventricle chamber (LV-chamber) made from PET is placed upstream the tube. The LV chamber is connected to the tube and to a reservoir. A valve (the mitral valve) is placed between the LV chamber and the reservoir to allow the flow towards the chamber but to prevent backflow into the reservoir again. A piston in the LV chamber is driven by a linear motor creating a pulsatile flow. Downstream the aorta another chamber (C) is placed. This C chamber simulates the systemic compliance in the set up. A resistance is placed upstream and a resistance is placed downstream the C chamber, to allow tuning of the required pressure in the aorta.

![Figure 2.2: Schematic representation of the in vitro experimental model.](image)

The LV-chamber pumps water through the artificial valve into the aorta and from the aorta into the systemic Windkessel components (with lumped parameters Rao, L, C and Rp representing aortic resistance, systemic inertance, systemic compliance and peripheral resistance, respectively). Coronary arteries branches of the aorta, passes the coronary artery flow probe, the arteriolar sphincter resistance Rar, and ends in the part of the set up called “coronary cylinder”. The coronary cylinder represents the last of the path done by the fluid from Rar until the venous outlet V. Myocardial lumped resistances are indicated by Rm1, Rm2 and Rp. All resistances indicated are manually adjustable clamps.[15].
2.3 The Valve Housing and the Junction

In both the set-ups (for steady/pulsatile flow) the valve is placed upstream the polyurethane pipe that represents the aorta. The valve, a 23 mm size bileaflet St. Jude Regent, is placed in the setup in the following way (fig 2.3): a device of the set-up called the Valve Housing holds a short polyurethane tube in which the valve is inserted and fixed. Downstream the Valve Housing another piece of the set up is mounted, the Junction, which is connected to the aorta. A picture of the Valve Housing mounted to the Junction is shown in figure 2.3.

![Figure 2.3. Valve Housing and Junction. The valve is held in the short polyurethane tube placed in the Valve Housing part. Downstream the valve housing the Junction part is assembled (the white one on the right). These two pieces could be blocked together and reopened in order to rotate the Valve Housing with respect to the Junction downstream. The junction was connected to the aorta tube.](image)

The Junction has several holes (2.7 mm diameter) arising from different position with respect to the valve. These holes can be closed with caps (the red ones in picture) or connected to rubber tubes which represent the coronary arteries. The coronary arteries setup part will be presented later, in the flow experiment set-up paragraph (2.5.1)
2.4 Pressure measurements setup

For pressure experiments series one of the closure caps in the Junction piece (fig 2.3) is removed and a steel needle is led through the hole into the Junction piece. The figure 2.4 shows two pictures of the Junction after the insertion of the needle. The needle is bent with a 90 degrees angle.

![Figure 2.4: Bent steel needle and its position with respect to the valve.](image)

The photo on the left (A) shows the Junction piece with the needle inside. The needle is held by a device with three branches that avoids the leakage. The photo on the right (B) shows a view of the Junction and of the Valve Housing from downstream, the valve and the position of the needle with respect to it can be seen.

The needle is held by a device (the transparent three-branched one in fig 2.4 A). The needle can be pushed inside the Junction or pulled back. In this way the height of the needle can be changed with respect to the axis of the valve. In figure in fig 2.4 B the tip of the needle is facing the area between the leaflets of the valve. It is then possible to pull it up increasing its height and make it facing the upper major orifice of the valve, or push it down, decreasing its height and let it face the lower major orifice of the valve. It is also possible to rotate the needle. In figure 2.4 B the needle is pointing to the center of the valve but can be rotated to the right, to point at the right hinges of the leaflets or rotated to the left and pointing at the left hinges. A Radi Wire pressure sensor is led through the needle until the sensor of the pressure wire reaches the tip of the needle. Two kinds of needles are used: front open needles and needles with side holes.
2.4.1 Open Needle

Figure 2.5 shows the shape of the front open needle. The tip of the needle is open.

![Diagram of Front Open Needle](image1)

*Figure 2.5 Front open steel needle. The Radi wire is inserted in the needle and the sensor is positioned in the tip of the needle just at the opening of it.*

The front open needle measures pressure of the fluid at stagnation point (at the enter of the needle fig 2.5)

2.4.2 Side Hole Needle

A picture of the side hole needles is shown in figure 2.6. The Radi wire is led through the needle and pulled until the sensor goes beyond the hole and lays in the tip of the needle.

![Diagram of Side Hole Needle](image2)

*Figure 2.6 Needle with side hole. The pressure sensor of the radi wire is positioned after the hole, at the tip of the needle.*

The side hole do not represent a stagnation point for the flow. The use of the two different needles will be discussed in the methods part.
2.5 Flow measurements set-up

2.5.1 The coronary circuit

The red closure caps in fig. 2.3 can be removed and can be replaced with the coronary arteries circuit. The coronary arteries circuit consists of two rubber tubes (3 mm diameter) which represent the coronary arteries (fig 2.7). The two rubber tubes (the coronary branches in the set-up) converge in a Y junction that conveys the flow in a single tube.

![Figure 2.7: Coronary circuit. It consist in two rubber tubes (the two branches) of the same length which converge in third tube thanks to a Y junction that conveys the flow in the last tube. These two branches arise from the orifices in the Junction part (fig 2.3). Choosing different orifices it is possible to create different angles between the two branches. By clamping each of these branches separately it is possible to measure the flow through the separate branches arising from different positions with respect to the prosthetic valve.](image)

By clamping each of these branches separately it is possible to measure the flow through the separate branches arising from different positions with respect to the prosthetic valve.
2.5.2 Coronary resistance

The resistance of the coronary circuit is obtained in two ways:

- with a constant resistance
- with the coronary cylinder

In the first case, the coronary circuit is connected to a purely resistive system, whose resistance can be changed by manually adjusting clamps.

In the second case the rubber tube after the Y-junction is connected to a particular part of the set up that will be called “coronary cylinder” (fig 2.8). This part is used to mimic coronary physiology.

![Coronary cylinder](image)

*Figure 2.8: Coronary cylinder. The main chamber is kept at the same pressure of the left ventricles, in the rubber tubes inside flows the fluid from the coronary branches.*

The coronary cylinder simulates the effect of the squeezing of the heart on the coronary arteries, during systole. Using this device a physiologic coronary pattern can be achieved i.e. high flow in diastole and low flow in systole.

The coronary cylinder consists of two collapsible tubes through which the flow from the coronary branches is directed. The tubes are placed in a chamber. During the cardiac cycle the pressure in this chamber has the same value as the ventricular pressure. So the pressure in systole causes the collapsible tubes to obstruct the flow while in diastole the tubes are released and the flow increases. An RC model of the cylinder is sketched below. (Fig.2.9). By tuning the three resistances R1 R2 and R3 it is possible to mimic physiological coronary flow.
Figure 2.9: Coronary cylinder electrical model. R1, R2 and R3 can be tuned up. Rv1 and Rv2 are resistances that change with regard to the pressure in the left ventricle (the pressure in the left ventricle causes a reduction of the diameter of the collapsible tubes).
2.5.3 The rotation device.

The rotation device has been designed to solve some of the problems induced by the previous set up. When used (experiments described in 3.3.3), the rotation device replaces the valve housing (see fig 2.2) in the set-up during the experiment on coronary flow. The limitations that this new piece tries to overcome can be divided in limitations in use and geometry limitations.

Limitations in use:
In the Valve Housing piece (fig 2.3) the valve was held in the rubber tube and tided in it. Therefore it was not possible to rotate the valve during the experiments. To set around this problem the only chance to measure the flow for the two orientation of the valve was clamping the coronary branches arising from the different positions (A and B in fig 3.7). As a result, in fact the orientation’s effect of the valve was evaluated changing the coronary position with respect of the valve and not changing the orientation of the valve itself. Moreover, the clamping procedure usually took a certain amount of time, during which the pressure values could change in the set up. More important, the clamping procedure could lead to errors in measurements because the manual clamping may change the position of the coronary branches and their resistance. In general the system gave evidence to be sensitive to any external action affecting the result of the measurements. The rotation device allowed performing the experiments faster and with a large reduction of these actions on the setup.

Geometry limitations.
The first limitation of the Valve Housing and the Junction was that the coronary branches arose from 3 cm downstream from the valve. This is not a physiological situation and this difference might change the results. In the rotation device the coronary branches arise 1.5 cm downstream from the valve. The second limitation was the shape of the aortic root. The section of the Junction in which the coronary branches arose was cylindrical, which again represents a non physiological situation. The rotation devices attempts to replicate the anatomy of the aortic root and of the sinuses of the Valsalva.

The design of the rotation device is given in fig 2.10. The shape of the external cylinder (in grey) is build to fit in the other set up components.
Figure 2.10: Rotation device design.
The rotation device is composed by five pieces. A housing (in grey) two cylinders (in yellow) the valve rotator and the valsalva root (in blue).

The two cylinders hold the valve rotator and the valsalva root in the way that they can reciprocally rotate. The valve is placed in the valve rotator. As mentioned the distance between the valve and the coronary ostium is 1.5 cm. The cavity in the valsalva root has been obtained drawing a sphere with a 17 mm radius. This shape has been chosen because it approximates the anatomy of the sinuses quite well. Considering an aortic root with the valve closed under a static pressure of 100 mmHg these dimensions are in an error range of 1 mm. [6]

The natural Valsalva root has three coronary ostia. Considering a section of the natural valsalva root these three coronary ostia arise with 90 and 120 degrees with respect to one each other, see fig 2.12.

In this way it was possible to use the coronary ostia that where 90 degrees apart to study the orientation A versus B. Using the coronary ostia that where 120 degrees apart it was possible to replicate Kleine’s experiments orientating the valve in the two positions, with the leaflets in the middle of the coronary arteries (m) or parallel (p). see fig 2.13.
Figure 2.13: The holes shifted by 120 degrees can be used to replicate the Kleine experiment orienting the valve in position M or P.
3 Methods

3.1 Flow rate and waveforms

The flow through the aorta could be chosen between steady and pulsatile.

The steady flow, as mentioned in description of set up (chapter 2.1), was provided by a system of barrels placed at different heights. The flow rate could be increased up to circa 30 l/min by adjusting the resistance downstream the aorta (Rao in fig 2.1).

The pulsatile flow was provided by a motor, moving a piston in the LV chamber, (paragraph 2.2). It was possible to program the motor to produce a particular wave shape or to change the duration of each cycle. The combination of both, cycle duration and wave shape, was used to mimic the cardiac output in resting and in exercise condition.

For resting condition the wave shape used has been plotted in fig 3.1. The graph in 3.1 shows the total volume of water which the LV chamber (see fig. 2.2) ejects in each moment of the cardiac cycle since the piston is completely backwards. The position in which the piston is completely backwards is taken as the start of the cardiac cycle. In the first part of the graph, (from zero until 0.3 sec) the piston moves forward and the total ejected volume increases, reaching the peak of 62.5 millilitres. In this part of the cycle the water flows in the aorta pumped by the piston that is moving forward. This is the part of the systole in our set-up the aortic valve is opened and the mitral valve is closed (see fig. 2.2). In the second part the ejected volume is decreasing (from 0.3 until 0.8 sec) and returns back to zero millilitres. In this part the piston is moving back, sucking back the water and the LV chamber is refilled, that is why the total amount of ejected volume is decreasing in the graph. This is the part of the diastole in our set up, the aortic valve is closed and the mitral valve is opened, therefore the water flows from the reservoir in the LV chamber.

![Diagram](image)

**Figure 3.1 Volume which moves from the LV chamber because of the piston displacement during one cycle in resting condition. In the first part (until 0.3 sec) the aortic valve is opened, the piston moves forward and the water moves from the LV chamber to the aorta. Therefore, in this first part, the volume that has left the LV chamber increases until 62 ml**
that represents the volume moved by the piston during the entire systole. In the second part (from 0.3 sec until 0.8 sec) the piston moves back, the aortic valve is closed, the Mitral valve opens, and the LV chamber is refilled with the water from the reservoir. Therefore the volume moved by the piston from the start of systole decreases and reaches zero at the end of diastole.

Figure 3.2 shows the flow during cardiac cycle. During systole the piston moves forward and the water flows from the LV chamber into the aorta (it can be seen the peak of systole at 0.12 sec). During diastole the flow moves back and the water moves from the reservoir into the LV chamber, refilling it.

![FLOW DURING ONE CYCLE (RESTING CONDITIONS)](image)

\[ T_c = 0.8 \]

That for \( T_c = 0.8 \) gives \( T_s = 0.277 \).

The heart rate was set to 75 beat per minute so the time of cardiac cycle (Tc) was 0.8 seconds. As can be seen in figure 3.1 the systole lasts for 0.284 seconds. Therefore in our set up the time of systole (TSs) is 0.284 seconds.

This duration of time can be compared with the relationship between systolic and cardiac cycle durations as described by Katz and Feil (1923) (eq. 3.1).

\[ T_s = \sqrt{0.096T_c} \]

That for \( T_c = 0.8 \) gives \( T_s = 0.277 \).

This value for \( T_s \) is very close to the value TSs in our set up which means that our set up well approximates the time of systole and diastole found in literature.
The stroke volume was chosen about 65 ml / beat, therefore the cardiac output (65 ml/beat * 75 beat/minute) results to be about 5 liters per minute, which represents a realistic situation in resting conditions.

For exercise conditions another shape of flow was made, which is represented in fig 3.3.

![Volume moved from the LV chamber by the piston displacement (exercise conditions)](image)

*Figure 3.3: Ejected volume during one cycle in exercise condition. The duration of the cardiac cycle is 0.5 seconds circa. The ratio between the time of systole and diastole is calculated applying eq 3.1.*

The heart rate was set to 125 beats per minute so the time of cardiac cycle (Tc) was 0.48 seconds. The stroke volume was changed to 75 ml to obtain an increased cardiac output. The cardiac output with these parameters values was ~ 9 liters per minute, corresponding to a moderate exercise. It should be noticed that also the ratio between time of diastole and time of systole was changed, applying eq. 3.1.
3.2 Pressure experiments

3.2.1 Steady/ pulsatile flow and open needle (5 sites)

For this series of experiments in the cross section area downstream the valve 5 sites were chosen to measure pressure. The choice of these sites was to investigate the pressure differences, across a section, of the fluid jets downstream the valve. Measurements in each site were intended to point out the differences in fluid dynamic situation due to the geometry of the valve.

The open needle works like a Pitot tube and measures pressure of the fluid at stagnation point. This means that the sensor is measuring the static pressure in our system plus an additional term. Starting from eq 1.2 and considering the first term we obtain:

\[ P + \frac{1}{2} \rho V^2 = P_{tot} \]  \hspace{1cm} (3.1)

Where \( P \) is the pressure that the sensor would measure if it moved with the same velocity \( V \) of the fluid and \( P_{tot} \) is the pressure that our sensor would measure working as an ideal Pitot tube). This additional term (the second part of the first term in eq3.1) is given by the velocity of the fluid layers and is called the kinetic component. At the entrance of the needle the fluid has zero velocity (the stagnation point in fig 2.5) and the kinetic component of the fluid is converted in pressure.[17]. It has to be noticed that \( V \) depends on the site of measure, as can be seen comparing figure 3.4 with figure 1.9b.

For steady flow rates from 5 to 25 liters per minute (l/min) have been chosen. For each of the sites the pressure in the needle has been measured for 3 seconds sampling at 30 Hz. Then the mean of each measurement was computed for each site.

For pulsatile flow a cardiac output of 4.5 liters per minute was chosen with a frequency of 75 beats per minute and a stroke volume of 65 ml per beat. These values were used to represent the resting conditions. The waveform that was used in these experiment is plotted in fig 3.1. For each site the pressure was measured for 2 cardiac cycles sampling at 256 samples/cycle (320 Hz).

For both of the series above the experiments have been conducted at 1 and 3 cm distance downstream from the valve.
3.2.2 Pulsatile flow and side-hole needle (11 sites)

For this series of experiments in the cross section area was divided in 11 sites.

![Figure 3.5: Sites of pressure measurement with needle with side hole](image)

These sites of measurement had the intent to investigate any differences in fluid dynamic situation (with regard to pressure and velocity) due to the rotational antisymmetry of the valve. Sites 1-5 and 6-7 were chosen to compare the flow downstream the major orifices with the flow downstream the hinges. Sites 1 and 5 face the area of major flow and therefore in the peak of systole in these areas higher velocities will be present. Sites 6 and 7 face the hinges of the valve and in peak of systole in these areas lower velocities will be present. Sites in the middle (i.e. from 2 to 4) were chosen to investigate the effect of the leaflets on the developing of the velocity profile during the cardiac cycle. This series of experiments has been carried out performing experiment in more sites than the previous series. However as can be seen, the 11 sites are the obtained projecting the 5 sites with respect to a vertical symmetry axis (which crosses sites from 1 to 5) and then projecting the sites with respect to an horizontal symmetry axis (which crosses sites from 7 to 6).

The reason is that when the needle is in position 1,2,3,4,5 the side hole does not represent a stagnation point for the fluid, therefore the kinetic component (the velocity of the fluid) does not affect our measurements.[17] In the other sites, the side hole is affected by the fluid velocity, although this influence is much less than in the experiments with the front open needle. Since this the sites symmetric with respect to the vertical axis have been used to correct the measurement, as will be explained later in this paragraph, correction by side position (kinetic component).

Four series of measurement were performed. During each series for resting conditions pressure in the sites was measured for 10 cardiac cycles, sampling at 256 samples/cycle (320 Hz). During each series for exercise conditions pressure in the different sites was measured for 10 cardiac cycles, sampling at 512 samples/cycle (1066 Hz). During two of the four measurements pressure was also measured in the left ventricle by using a pressure probe. During the other two measurements, the pressure probe was inserted in the aorta. The reason of measuring the pressure in aorta and in the ventricle is in the correction of the data obtained as will be explained later,(Correction by the ventricular/aorta pressure measurements).

After the acquiring, the data were corrected and averaged as explained below. Since the differences measured were small it was important to make correction for height and kinetic component.
**Correction by height:**
The height in the different sites affects the mean pressure in each site. In example between site 1 and site 5 exists a difference in pressure of ~1.5 mmHg due to the pressure exerted by the water. Therefore, each measurement has been corrected in regard to the different height. The correction was made adding to the pressure measured in each site the term:

\[ P = \rho gh \]  \hspace{1cm} (3.2)

where \( \rho \) is the density of water, \( g \) is the acceleration of gravity and \( h \) is the height between the site 1 and the site of measurement.

**Correction by side position (kinetic component):**
During the data analysis a systematic difference among the sites on the side was noticed. In sites 6, 8 and 10 pressure was always lower than in sites 7, 9, 11 in the four series. This was explained considering that the position of the side hole with respect to the flow can affect the pressure measurement. See fig below.

![Diagram](image)

*Figure 3.6: Position of the side hole affects the measurement, for sites 7, 9, 11, the hole is facing the flow and a small part of the kinetic component of pressure is measured. For sites 6, 8, 10 the same part of the kinetic component is subtracted.*

Therefore, considering the symmetry of the system, each side sites have been averaged with its correspondent (6 with 7, 8 with 9 and 10 with 11) in order to erase the kinetic component of pressure.
**Correction by the ventricular/aorta pressure measurements:**
Pressure in the set up could change slightly during the experiments. These changes could occur for different reasons. One of the reasons was the creeping of the pipe. Other reasons were variations in the level of water in the C chamber or small variation of the resistances due to the loosening of the clamps. Pressure experiments with the 11 sites usually took a long time and sometimes it was possible to see the effect of these variations in the measured pressure. Due to the overall variations in the whole set up the measurements in the different sites were affected. Therefore the pressure measured in the aorta/ left ventricle with the pressure probe was taken as a reference value to correct the pressure measurement in the sites.

**Average, the 10 cycles:**
In order to make the results easier to be read, the ten cycles taken for each site were averaged. It has to be reported that during the experiments each cycle of the pressure was similar in the 10 cycles.
3.3 Flow experiments

3.3.1 Constant resistance

A constant resistance for a coronary artery is not a physiological situation in coronary perfusion but offers the chance to investigate coronary flow without the influence of the beating heart. The coronary circuit was connected to a purely resistive system. The resistance of this system was controlled by a clamp, and kept constant during the experiments. The flow probe was placed after the Y Junction in fig 2.7.

The coronary branches were inserted in the Junction part (fig 2.3). The coronary branches arose from two different position with respect to the valve. Figure 3.7 shows the two positions, marked as A and B.

![Figure 3.7: Positions of arising for coronary branches. A position faces the major orifice, B position faces the hinges of the leaflets.](image)

Position A is the position in which the ostium of the coronary branch is facing the major orifice of the valve. Position B is the position in which the coronary branch is facing the hinges of the leaflets. The coronary branches were always inserted during the experiments, therefore differences in flow for the two positions were measured clamping one of the branches and let the flow run in the other. As can be seen position A corresponded to site 1 and position B corresponded to site 6 for the pressure measurement with 11 sites and side holes needle (paragraph 3.2.2).

Flow was measured in the each coronary branch for position A and for position B. Flow measurements were performed 15 times placing the valve with the leaflets in horizontal position (horizontal valve) and 16 times placing the valve with the leaflets in vertical position (vertical valve). The reason of measuring flow for the two positions A and B in two different situations (horizontal/vertical valve) is that was not possible in the set up to rotate the valve with respect to the coronary branch, on the contrary the coronary branch had to be switched to be in position A or B. Therefore, the experiments have been carried out the first time placing the valve as horizontal and the second time placing the valve as vertical to ensure that the switching of the branch did not play a role in the differences in measured flow. During each of this two series the flow was measured in position A and B alternating the position of the coronary branch from A to B and from B to A.
In each measurement flow rates were acquired for 8 cardiac cycles sampling at 256 samples/cycles (320Hz). Then for each series the average of flow rates for the two positions during the 8 cycles was computed.
3.3.2 Coronary resistance

For the coronary flow measurements with variable resistance, the coronary branches were connected to the coronary cylinder (see fig 2.8). The flow probe was placed at the ostium of the coronary cylinder. Four series of experiments were carried out placing the valve with the leaflets in horizontal and vertical position. During each series flow has been measured for 8 cycles in position A and B, sampling at 256 samples/cycle (320Hz). Mean flow has been computed by averaging the values obtained during the 8 cycles.

3.3.3 Rotation Device

Flow experiments in flow with the rotation device were conducted in the following order:

1) Single/ double coronary branches.
2) Normal/hyperemia coronary resistance
3) Resting /exercise conditions.

Single/ double coronary branches refers to the use one coronary branch arising from position (A vs. B same as in 3.3.2) or to the use of two coronary branches arising in position M or P in respect to the valve. Normal/hyperemia coronary resistance refers to the resistance offered by the coronary cylinder, in the second the resistances were decreased leading to higher coronary flows. Resting /exercise conditions refer to the cardiac output and heart rate used during the experiments. Resting conditions correspond to 4.5 l/min and a heart rate of 75 bpm (beats per minute). Exercise conditions correspond to a cardiac output of 9 l/min and a heart rate of 125 bpm. The following experiments were performed.

- Flow with one branch, normal coronary resistance, resting conditions.
- Flow with one branch, hyperemia coronary resistance, in resting conditions
- Flow with double branches, normal coronary resistance, resting conditions.
- Flow with double branches, hyperemia coronary resistance, resting conditions.
- Flow with one branch, normal resistance, and exercise conditions
- Flow with double branches, normal coronary resistance, and exercise conditions.
- Flow with double branches, hyperemia coronary resistance, and exercise conditions

In each of the experiments four measurements were performed measuring the flow for 32 cycles. In two of the measurements the experiment started with A or M position (depending on the experiment) and, after 16 cycles, the valve was rotated in position B or P (depending on the experiment) respectively. In the other two of the measurements, the starting position B or P was switched to A or M after 16 cycles.
4. Results:

4.1. Pressure experiments

4.1.1 Pressure experiment with 5 sites in steady/pulsatile flow with open needle

The graphs in fig 4.1 show the results for pressure experiments in steady flow condition (see fig 3.4 for the location of the sites). This results have not been corrected by the height. The differences among the sites are in the range of 5 mmHg. For increasing flow rate, the mean pressure of the sites decreases. For increasing flow rate differences between sites increase. The reasons these differences will be discussed in chapter 5.

![Graph (a)](image1.png)

![Graph (b)](image2.png)

*Figure 4.1.a and b:* Mean pressure in the 5 sites for steady flow. The distance of the pressure sensor downstream from the valve is 1 cm (a) and 3 cm (b). In X axis is reported the flow rate. In the Y axis is reported the pressure in mmHg. The different colors of the triangles refers to different sites as explained in the legend on the right side.
The graphs in fig 4.2 show the results for pressure experiments in pulsatile flow condition. The most remarkable pressure differences are seen at peak of systole. Differences are in the order 7-8 mmHg at maximum.

**Fig 4.2.a and b:**
Pressure patterns in the 5 sites for pulsatile flow. The distance of the pressure sensor downstream from the valve is 1 cm (a) and 3 cm (b). In X axis is reported the time. In the Y axis is reported the pressure in mmHg. The different colors of the lines refers to different sites as explained in the legend on the right side.
4.1.2 Static pressure measurements in pulsatile flow 11 sites

In the following graph are reported the pressure patterns in the 11 sites for the 4 measurements. The 10 cycles are averaged. The results are height corrected and normalized to ventricular/aorta pressure.

*Figure 4.3: Pressure patterns measured in the 11 sites for the four measurements. In the x axis are reported the 11 sites, Y axis represent the time as duration of one cardiac cycle (0.8 sec). On the Z axis has been reported the average of the 10 cycles.*
In the following graph one of the measurements (measurement 3) is plotted. Values are corrected for the height and for the value measured with the pressure probe. Side sites have been averaged to exclude of the kinetic component of pressure as explained in the methods chapter. As can be seen, the pressure patterns show the same shape for the different sites. The differences in pressure in the peak of systole are in the order of 2 mmHg (refer to fig.3.5 for the location of the sites).

Figure 4.4. Pressure patterns for the third measurement. The 10 cycles have been averaged for each site. Different colors belong to different sites. The notations 6/7, 8/9, 10/11, indicate that pressure patterns in the sites 6 and 7, 8 and 9, 10 and 11 respectively have been averaged.
In the last graph the mean pressure during the cycles for all the measurement is reported. After the corrections (see methods section) for every measurement the mean is computed for each site. The mean of the four measurements is plotted with error bars. Each error bar in the graph reports the min and the max of the four measurements for that site. Differences do not exceed 1.5 mmHg.

Figure 4.5. The squares represent the mean pressure during the 10 cardiac cycles for the 4 measurement. The x axis reports the different sites, as in the last graph notations 6/7, 8/9, 10/11, indicate the average between sites 6 and 7, 8 and 9, 10 and 11 respectively.
4.2 Flow experiments

4.2.1 Experiments on flow with constant resistance

For each orientation of the valve 15 measurements for position A and B with horizontal valve and 16 measurements for position A and B with vertical valve were performed. Results are plotted in the graphs below.
Figure 4.6: Average coronary flow over 8 cycles measurement for constant resistance. A and B represent the two positions as explained in the methods section. Each circle/square represents the average flow in each of the measurements.

For the first series no the flows are quite the same. 
In the second series there is a slight difference 1 – 2 ml/minute.
4.2.2 Experiments on flow with variable resistance

In the following graphs the pressure and flow patterns are plotted obtained connecting the coronary branches to the coronary cylinder.

*Figure 4.7* pressure and flow patterns for variable resistance. The blue and the green lines are the flow in the A and the B position (see fig 3.7) respectively measured in ml/min (right Y axis). The red and cyan lines are the pressure patterns in aorta during the measurements and refer to the A and B position respectively. During the experiment the valve was placed with the leaflets in horizontal position.
It can be seen that the flow patterns are overlapping. The pressure patterns have been reported in order to show that during the experiments the pressure in the aorta was the same. The next graph shows the plots averaging the 8 cycles.
Figure 4.9 flow patterns for variable resistance. The blue and the green lines are the flow in the A and the B position respectively measured in ml/min.
The last graph shows the mean of the flows for each measurement.

In this series of experiments differences between the flows means are in the order of 1.5 ml/min at maximum. As can be seen the flow rates show to decrease during the series. This is due to the behavior of the coronary cylinder that presents certain instability.
4.2.3 Experiments on flow with rotation device

Graph description:

The top picture of the seven graphs below shows the results for the seven experiments (see paragraph 3.3.3). The part before the switching line shows the average of the first 16 cycles, the part after the switching line shows the average for the cycles from 17 to 32, in which the valve was rotated from A to B (see fig 3.7) position or back (during experiments with one branch) and from M to P (see fig 2.13) position or back (during experiments with double branches). For each experiment the number of the four measurement is reported (on the right).

The bottom picture (for experiments with single coronary branches) shows the average for the cycles in the position A and B (see fig 3.7). In blue (thick line) the average is represented for the cycles in position A and in red (thick line) the average for the cycles in poison B is represented. The dashed blue lines represent the measurements in position A while the dashed red lines represent the measurements in position B.

The bottom picture (for experiments with double coronary branches) shows the average for the cycles in the position M and P (see fig 2.13). In blue (thick line) is represented the average for the cycles in position M, in red (thick line) is represented the average for the cycles in poison P. The dashed blue lines represent the measurements in position M while the dashed red lines represent the measurements in position P.

The graphs show that flow in coronary branches is not affected by the orientation of the valve. Some differences can be seen among the measurements in the different positions (red vs. blue dashed lines) but the shape of the coronary flow remains similar for the different measurements. The averages of the measurements for the different positions (red /blue thick lines) are the same and their patterns are overlapping.
Flow with one branch, normal coronary resistance, resting conditions.
Flow with one branch, hyperemia coronary resistance, in resting conditions
Flow with double branches, normal coronary resistance, resting conditions

Average of the cycles from 1 to 16
Average of the cycles from 17 to 32

Average of the measurements

Flow in ml/min

Time in sec
Flow with double branches, hyperemia coronary resistance, resting conditions

Average of the measurements
Flow with one branch, normal resistance, and exercise conditions

Average of the measurements
Flow with double branches, normal coronary resistance, and exercise conditions

Average of the measurements

Average of the cycles from 1 to 16

Average of cycles from 17 to 32
Flow with double branches, hyperemia coronary resistance and exercise conditions

Average of the measurements

Average of the cycles from 11 to 16
Average of cycles from 17 to 32
5. Discussion of the results:

5.1 Pressure

The experiments with steady/pulsatile flow in the 5 sites with open needle showed differences in pressures for the different sites. These differences ranged from ~2 mmHg for low flow rates (5 l/min) up to ~5 mmHg for high flow rates. Results also show a decrease of the mean pressure in the sites for increasing flow rates (25 l/min).

This can be explained considering that the increasing the flow means increasing the velocity in the aorta. Therefore for equation 1.5 the mean pressure has to decrease when the velocity increases.

As explained before the open needle worked as a Pitot tube and a kinetic component was added to the pressure measured. So it is important to compute the magnitude of this additional component due to the velocity profile and understand what part of the these differences belongs to the static pressure and what part in fact is due to the kinetic component.

Starting from the Bernoulli equation, eq. (1.5) we can derive:

\[
\Delta P = \frac{1}{2} \rho \Delta V^2
\]  

(5.1)

From which we can compute 1 mmHg of difference in pressure corresponds to 0.515 m/sec difference in velocity.

This means that, in steady flow conditions, assuming the static pressure as constant for two points, if we measure difference a difference of 1 mmHg between these two points with a Pitot tube then the difference of the fluid layers for these two points is 0.515 m/sec.

From equation 1.2 we can compute the velocities in our tube.

\[
Q = V^*A
\]  

(1.2)

Where Q is the flow A is the orifice area of the valve (3.45 square centimeters) and V is the mean velocity across the valve.

For Poiseuille flow (fully developed flow) the mean velocity (V) is half of the peak velocity (Vmax).

\[
V_{\text{max}} = 2V
\]  

(1.3)
Hence we obtain:

\[ V_{\text{max}} = 2 \frac{Q}{A} \]  

(1.4)

The following graph compares the peak velocities downstream the valve, computed with eq (1.4) with the kinetic component computed with eq. (5.1), starting from the differences in pressure measured for site 2 and site 3 at different flow rates 3 cm downstream from the valve (see fig. 4.1 b).

![Graph comparison between the peak velocities in aorta (blue line) and the kinetic component among site 2 and site 3 (red circles). The x axis reports the different flow rates. In the Y axis there are the velocities in m/sec](image)

This graph has to be read in the following way: if we take a peak velocity of 0.5 m/sec we see that the difference among site 2 and 3 is calculated to be about 0.3 m/sec. We can compare this graph with picture 1.8. In picture 1.8 the peak velocity refers to the major orifices (site 2). The velocities on the layers between the two major jets are more comparable to the site 3.

Looking at the ratio between these two velocities we can see that the same ratio is maintained in the graph. See in particular the matching of the two graphs for flow rate of 20 l/min. Therefore the differences among the sites can be most likely ascribed to the differences in velocities. Same consideration can be done for the results obtained in pulsatile flow. Notice (fig. 4.2) that the differences occur in the central part of the systole and in the first part of diastole. During the rest of the cycle the patterns are overlapping. We can explain this thinking that in the phase of the acceleration/deceleration the fluid is moving like a “piston” (plug flow profile) and there are no differences in the velocities of the fluid layers. In the frame of time around the time of systole, between the acceleration and the deceleration, differences in velocities start to develop among the layers as can be seen in the pressure patterns. The last consideration goes in regard to the two distances (1 and 3 cm downstream); slight differences in pressure patterns can be seen between the a and b pictures of figures 4.1 and 4.2 these differences might be due to the developing on the
flow profile along the tube. However the behavior of the velocity patterns distribution remains similar. The method with the open needle revealed to be inappropriate for the investigation of the static pressure. This method can be used to investigate the velocity profile of the fluid layers. It is important on this purpose to point out the accuracy of this kind of measurements. The pressure sensor has an accuracy in the range of 1 mmHg (see Appendix) even assuming that the real accuracy (as experts can confirm) is in fact in the range of 0.1 mmHg, this inaccuracy has to be taken into account. 0.1 mmHg is translated in 0.16 m/s that cannot be neglected if we consider the range of differences we are dealing with.

The second series of experiments with 11 sites were out with the needle with a side hole to reduce the influence of the velocities as explained in the method part. However the orientation of the needle (see fig. 3.5) still affected our measurement by the kinetic component in sites at the sides. The following analysis of the data (averaging the sites at the side) allowed erasing this error. The results obtained with side hole needle confirmed the consideration done for the previous experiments about the velocity influence.

Fig 4.4 shows the behavior of these patterns; we can see that the differences are in the order of ~2 mmHg during the cycle. An exception is the part before the peak of systole, where more pronounced differences can be observed. The underlying causes for these differences are not clarified yet. Looking at the values of the means of the measurements fig 4.4 we can see that there are no major differences in static pressure among the sites. Even the largest difference, between site 3 and 10/11 is in the order of 1.5 mmHg. This difference compared with the mean pressure in aorta is not enough to lead to alterations in coronary flow as long as we recognize in pressure the main driving force for coronary perfusion.

5.2 Flow:

The results for the flow experiments followed the results found for the pressure experiments. The flow experiments were carried out with increasing complexity of the setup. In the first experiments the coronary arteries were represented as a purely resistive circuit. In the second series of experiments the influence of the contraction of the heart was included. And in the third series of experiments the geometry was improved to follow the aortic root anatomy. In all the series the flow proved to not be affected by the orientation of the valve. The flow patterns are completely overlapping and the means among the measurement showed very small variations probably due to the measurement inaccuracy, unavoidable for this kind of setup.

Therefore for this kind of experiments we can state that the coronary perfusion is not affected by the valve orientation. This means that in our set up the differences in the fluid layers developed downstream the valve (due to the valve rotation) do not play a role in changing the coronary perfusion. The differences in velocities or the two orientations might not affect the flow in the coronary branches since the size of the branches is small with respect to the size of the aorta (see chapter 1.1). In this case the behaviour of the flow in the branches depending on the velocities might be likened to the dotted line in figure 1.4. The dotted line in figure 1.4 likely represents the situation in which our experiments are performed; small side branch with respect to the main branch. In the graph the dotted line refers to a ratio of 0.2, this means that the diameter of the coronary branch should be 0.1 times the diameter of the aorta. That is more or less the case of our set up in which the coronary branches diameter is 3 mm and the aorta diameter is circa 26 mm. The effects of turbulence on coronary flow have been not clarified yet. However, the results obtained show that in this kind of set up the orientation of the valve does not leads to changes in turbulence capable to affect coronary perfusion.
These results are in contradiction with the results found by Kleine [10] (see chapter 1.5). Kleine suggests that differences in coronary flow might be ascribed to the difference in turbulence with respect to the two orientations. It has to be noticed that in Kleine's study the A position (in which he measured higher coronary flow, figure 1.10) represents also the best hemodynamic orientation for the valve, in other words, the orientation that leads to less turbulence rates. Therefore Kleine concludes that:

"Implantation of the MHV in the optimum orientation, which was accompanied by the most physiologic flow with respect to downstream turbulence during ejection now led to the highest LAD flow rates" [10].

The best hemodynamic orientation had been investigated by Kleine himself in [12]. However, looking at the results in this work seems that the B orientation leads to less turbulence than orientation A. The following picture can be found in the same article.

St. Jude 23 mm, Top Systole

![Figure 5.2](image)

Figure 5.2 Kleine compares different orientation with respect to the level of RNS (Reynolds normal stress). RNS, measured by Kleine with the PDU (Pulsed Doppler Ultrasonography) has been taken as index of the rate of turbulence downstream the valve.

The first image corresponds to orientation B, because the two major orifices are facing the anterior and posterior wall of the aorta. As can be read the level of turbulence measured by Kleine is 5.2. The third image (90° angle) corresponds to orientation A. In this case Kleine measured a level of turbulence of 6.0, higher than in orientation B. Indeed seems reasonable that less turbulence occurs in orientation B because in this case the leaflets during systole are con crossing the area of major flow, which is placed towards the posterior wall of aorta.

Furthermore, Kleine in this work implanted two St. Jude valves and the results for the two valves with respect to the turbulence were different, with 45 degrees shift as can be see in one of the table of the same article.
As can be seen, the best orientation for the first St. Jude valve corresponded to a 0° angle (first image in figure) while for the second St. Jude valve, the best orientation corresponded to a 135° angle (fourth image in figure). The best orientation was calculated by Kleine as the mean of the turbulence values for the two valves with respect to the different angles.

Since this, the turbulence phenomena, investigated in this study, are not sufficient to explain the changes that might occur with regard to different orientations of the valve.

### 5.3 Limitations of the study

The limitations of this study consist in the impossibility to recreate every physiological condition and, since this, to take the results as fully representative of the in vivo situation.

One of the limitations is the geometry of the set up. The shape of aortic root has been recreated trying to reproduce the dilatation of the diameter in the first part of the aorta (see rotation device description). Although this can represent an improvement with respect to some in vitro studies, in which the sinuses resulted absent or roughly modelled [13], the aortic root in the set up is not perfectly bio morphed, and does not replicate in every detail the shape of the sinuses of Valsalva. Furthermore, the materials used to build the pieces in the set up are characterized by completely different stress-deformation behaviour [18,19]. The aortic root, presents a certain distensibility due to the presence of elastine fibres in the wall of the vessel [20]. This distensibility results in a compliance of the ascending aorta, and plays a role in the particular pressure patterns in aorta during the cardiac cycle [21,22]. The aortic root in our set up is rigid and presents no compliance. Another limitation of our set up is that it was not possible to recreate the typical asymmetric flow ejected by the left ventricle. The flow ejected in aorta during systole possesses spin and it is characterized an area of major flow in the first part of aorta [14]. Is not clear whether the particular shape of flow in aorta could lead to different results from the results obtained with symmetric flow.

### 5.4 Conclusions

The orientation of the aortic mechanical valve does not affect the coronary flow. Average flow and the shape of the flow patterns do not change as a consequence of the orientation of the valve. The differences in velocities of the fluid layers developed downstream from the aortic valve do not lead to differences in pressures in the cross section area of the aorta able to affect the coronary flow.
6. References:


[16] R. E. Hayes, K. Nandakumur and H. Nasr-El-Din


[20] Montevecchi, Biomeccanica, Dispense del corso


7. APPENDIX:

7.1 Acquisition setup

7.1.1 Radi wire pressure sensor

Radi wire pressure sensor has been chosen for pressure measurement for several reasons. In regard to the set up characteristics it showed important advantages. As first, it proved to be durable and capable to resist to mechanical stresses. This is an important feature taking in account that the Radi wire pressure sensor had to be led through long pipes and junctions that offered rough obstacles to pass.

Another important characteristic is given by its flexibility and its small diameter (see fig1 and 2). Only matching these two qualities was possible to lead Radi wire pressure through the steel bent needles. However the main purpose in using Radi wire sensor is that is one of the most used pressure wire in clinical application. Radi wire is commonly used during ordinary clinical procedure or exams, as the FFR measurement and CFR measurements.

One of the reasons of investigating coronary flow with flow probes performing pressure experiments with this wire is to prove if coronary flow changes can be predicted by the use of this instrument. Coronary flow measurement in vivo is not a simple procedure. It can be preformed by different methods but still remains quite invasive and inaccurate. Giving evidence that alterations in coronary perfusion can be suggested by measurements with this kind of sensor represents an important step in cardiologic tests.

![Radi Wire sensor dimensions](image)

*Figure 7.1: Radi Wire sensor dimensions.*
TECHNICAL SPECIFICATIONS

Pressure
Operating pressure range: -30 to +300 mmHg
Zero thermal effect: 0.3 mmHg/°C
Sensitivity thermal effect: 0.3%/°C
Zero drift: < 7 mmHg/h
Accuracy: +/- 1 mmHg plus +/- 1% of reading (-30 to 50 mmHg)
+/- 3% of reading (50 to 300 mmHg)
Frequency response: 0-25 Hz

Temperature
Range: 15 -42°C
Relative temperature accuracy: 0.05°C or 10% T, whichever greatest.
Frequency response: 0-7 Hz (Temperature mode) 0-25 Hz (CFR mode)

Electrical
Operating voltage: 100-240 VAC, 50-60 Hz

Dimensions and weight
Length: 175 cm
Diameter: 0.014 cm

Environment
Operating temperature: 15°C to 30°C (59°F to 86°F)
Relative humidity operating: 30-75%
Typical performance data in temperature range 35°C to 42°C measuring time less than 1 hour
combined PressureWire® Sensor and RadiAnalyzer®Xpress.
Radi physiological assessment system

7.1.2 Radi analyzer

Radi analyzer is a pressure wire interface. It is often used during clinical exams as a real time calculator of FFR.

Its advantage is showing the pressure patterns (phasic and mean pressure) in a time frame of 10 seconds. This feature proved to be quite functional in tuning up the set up.

Reaching a correct shape in pressure wave form before and during the experiment had main importance on flow measurement. In human circulation coronary flow is primarily driven by aortic pressure. Especially during diastole, when the most of the coronary flow occurs, the mean pressure value plays a first role in the coronary flow rate. The same behavior has been observed in our in vitro setup. Hence this interface was particularly useful in keeping under control the mean pressure and, at the same time try to achieve a physiological shape of pressure wave form in the set up. The shape of the pressure patterns could be modified by changing the resistance downstream and downstream the C camber (see Fig. 1 in Description of setup chapter). The effect in changing these resistances showed to be pronounced in the range of pressures we used to work. Furthermore, transitory due to any variation of the set up parameters had to be considered since they could deeply affect the pressure values during measurements. By this interface was possible to control these two effects and tune the setup in reasonable time.

The time of tuning up (and the last of the experiments) was an important point. It has been observed that polyurethane pipes (aorta) presented creeping. This affected pressure pattern by an increasing in diastolic pressure and in a less pronounced peak of systole.
TECHNICAL SPECIFICATIONS

Pressure signals
Pressure range -30 to 300mmHg
Accuracy ±2mmHg
Frequency response 0-25Hz or higher

Electrical specifications
Classification Class 1
Isolation Cardiac Floating
Defibrillation proof 5kV
Operating voltage 100-240V 50-60Hz
Rated current 5.5A
Fuses 2 x T2A/250V

Dimensions
Height x Depth x Width 32cm x 12cm x 36 cm
Weight 8 kg

Environmental conditions
Operating temperature 15°C to 30°C
Transport temperature -40°C to 70°C
Storage temperature Room temperature
Humidity, operating 30-75% rel

7.2 Amplifiers:

PICAS V2.6 Peekel:

PICAS V2.6, Peekel Instruments was used to amplify the input signal from the Radi analyzer and from the pressure sensor.

TECHNICAL SPECIFICATIONS

Carrier frequency inputs of the CA2CF-card
General
Typical accuracy class 0.1%
Bandwidth (-3 dB) 2000 Hz
Maximum cable length: 500m
Sensor connection 2-, 3-, 4-, or 6-wire configurations

Bridge supply (transformer-isolated)
Supply voltage 0.5... 5V (adjustable)
Voltage accuracy ± 0.05%
Frequency 5 kHz
Frequency accuracy ± 1%
Load 60... 1000 ? 0.1%
1000... 3000 ? >0.1%
Internal bridge-completion ½- bridge und
¾- bridge 120 ? / 350 ?

Measuring input (transformer-isolated)
Ranges (@5V excitation): ± 100 µV/V,..., ± 1 V/V
Input Filter: (High pass) > 500 Hz
Max. Common Mode Voltage 200V
Common Mode Rejection (50 Hz) >120 dB
Serial Mode Rejection: >66 dB
Capacitive input overload max. 7x range permissible
Special input filtering for noise reduction

Balance control
R-balance +/- 65 mV/V
C-Balance at 120 Ω bridge up to 10 nF
Output
Full scale voltage +/- 10 V
Protection long-term short circuit allowed
Maximum capacitive load 10 nF
Maximum cable length 100 m (@100 pF/m)
Frequency (-3 dB) < 2000 Hz
Filter type 7-pole low pass Butter worth -42 dB/Octave

Analog inputs of CA4AI-card

General
Typical accuracy class 0.1%
Bandwidth (-3dB) 10 Hz
Sensor connections 2-, 3-, or 4-wire configurations

Sensor supply:
Voltage: 5V ± 0.1% (max. 50 mA)
(Maximum for 4 channels together is 100 mA)
Current: 1mA ± 5% (max. 7,5kΩ)
Power for active sensors 24VDC (max 80mA)
(galvanic separated from inputs)

Input:
Measurement range : Voltage: ± 20 mV - ± 10V
Current: ± 5 mA - ± 100 mA
Resistor 100Ω - 7500Ω
Temperature PT100 -200 - +590 °C
PT1000 -200 - +590 °C
Type B +250 - + 1820 °C
Type E -200 - + 1000 °C
Type J -200 - + 1200 °C
Type K -200 - + 1370 °C
Type N -200 - + 1300 °C
Type R - 50 - + 1760 °C
Type S - 50 - + 1760 °C
Type T - 50 - + 390 °C
Cold Junction Compensation with a PT100 on channel 1 of the CA4AI-card.
Input filter (-3 dB) 10 Hz
Filter type: 2-pole low pass Butter worth
Input resistance: 10 MΩ
Max. input voltage: ±35V
Max. input current (only is current mode): 120 mA
Common Mode voltage ±12V
The CA4AI board does not have an analog output for each input channel!!

Controller Boards
PB6000 PB6100
A/D-converter 16 Bit
Amplifier calibration per Software and D/A-converter
Synchronization of carrier frequency digital (with other PICAS units)
Interfaces 1x RS232
1x RS485
1x USB V1.1
Digital outputs (solid state switch)
for trip generation
max. 48VAC/DC / 300mA
Max total conversion speed: 100 Hz 20.000Hz
Measurement value storage 29.000 values 500.000 values

Housing
PICAS 250 x 330 x 110 mm (B x T x H)
Power supply 100 - 240 VAC / 50/60 Hz
Operating temperature 0 -- +50°C
T420 Transonic flow meter

GENERAL FEATURES
Weight/ Size 5.125” high x 4” wide x 12” x 9.062” deep
2.2 lbs.
Module is 2 console slots (20HP) wide.

AUTOMATIC FLOWMETER ADJUSTMENTS
Probe size identification and corresponding flow output ranges (see probe tables)
Volume flow calibration of applied probe

SELECTABLE SCALE
Low Range increases flow gain by a factor of 4
Filter Properties 0.1, 10, 40 Hz: 2nd order Butterworth, with a third passive pole
at 160 Hz 160 Hz: 3rd order Butterworth
Polarity of Flow Invert inverts polarity of analog flow outputs and flow displays
Zero Flow Adjust momentary push button recessed to avoid inadvertent adjustment of zero flow reading

7.3 Flow sensor

Figure 7.2: Transonic flow probe.

A Transonic® perivascular Flowprobe consists of a probe body which houses ultrasonic transducers and a fixed acoustic reflector. The transducers are positioned on one side of the vessel or tube under study and the reflector is positioned at a fixed position between the two transducers on the opposite side, see fig. 8.

An electrical excitation causes the downstream transducer to emit a plane wave of ultrasound. This ultrasonic wave intersects the vessel or tubing under study in the upstream direction, then bounces off the fixed "acoustic reflector," again intersects the vessel and is received by the upstream transducer where it is converted into electrical signals. From these signals, the flowmeter derives an accurate measure of the "transit time" it took for the wave of ultrasound to travel from one transducer to the other. The same transmit-receive sequence is repeated, but with the transmitting and receiving functions of the transducers reversed so that the flow under study is bisected by an ultrasonic wave in the downstream direction. The flowmeter again derives and records from this transmit-receive sequence an accurate measure of transit time. The transit time of ultrasound passing through a conduit is affected by the motion of liquid flowing through that vessel. During the upstream cycle, the sound wave travels against flow and total transit time is increased by a flow-dependent amount. During the downstream cycle, the sound wave travels with flow and total transit time is decreased by the same flow-dependent amount. The Transonic flowmeter subtracts the downstream transit time from the upstream transit time utilizing wide-beam ultrasonic illumination. This difference of integrated transit times is a measure of volume flow.
Acoustical Coupling

Highest accuracy with ultrasonic transit-time flowprobes is achieved when the ultrasound signal is transmitted under uniform acoustic conditions. This occurs when the acoustic properties of the coupling media and tissue are stable and most closely match the acoustic properties of the liquid being measured (see figure 9).

The gel used contained 98.5% of water, providing an excellent matching with the acoustic properties of the water.

The flow probe measurements showed to be affected also by the position of the conduit in the area between the reflector and the transducer. Deflections of the coronary flow branches in this area lead to an increasing in flow measurements. Therefore a cast of agarose gel was used to keep the branch steady in the flow probe lumen.