UNIVERSITA' POLITECNICA DELLE MARCHE

FACOLTA' DI **INGEGNERIA**

Corso di Laurea magistrale **in Biomedical Engineering**

DESIGN AND DEVELOPMENT OF A TEST BENCH BASED ON ADDITIVE MANUFACTURING FOR THE STUDY OF PATIENT-RELATED TRANSCATHETER AND VALVE-IN-VALVE AORTIC PROSTHESIS

Supervisor:

Prof. **Lorenzo Scalise**

Co-supervisor: Chiar.mo/a

Prof. **Paolo Castellini**

Tesi di Laurea di:

Alessia Caputo

A.A. **2020** / **2021**

Summary

1. Introduction 1

1.1 Anatomy and Physiology of the heart and systemic circulation 2

1.2 Cardiac prosthetic valves 9

1.3 Transcatheter aortic valve implantation and Valve-in-Valve 21

1.4 State of the art of test benches for transcatheter aortic valves 23

2. Materials and Methods 28

2.1 Concept design of the bench 29

2.2 Applicable measurements techniques on the test bench 31

2.3 From physiological parameters to the preliminary design of the bench 32

2.4 Realization of test bench 35

2.5 Extraction of anatomical components 38

2.6 3D printing of anatomical components 40

3. Results 48

4. Discussion and Conclusion 54

5. Bibliography 60

1. Introduction

This thesis work, carried out at the Dipartimento di Ingegneria Industriale e Scienze Matematiche, has as its objective the design and the development of a test bench for the evaluation of the hemodynamic performance of Valve-in-Valve cardiac transcatheter aortic valves.

The contest in which the thesis is placed is the medical one, particularly focused on the cardiac field. In the last years, the introduction of new minimally invasive surgical techniques for heart valve implantation, in substitution to more dangerous open-heart operation, lead to the development of innovative test bench for the transcatheter aortic valves. The need for cardiac surgeons to test biological aortic valves before implanting them into cardiopathic patients drew the interest of bioengineers and experts in fluid dynamics. In particular, the interest is focused on the study of the hemodynamic of Valve-in-Valve and transcatheter aortic implantation valves.

The bench has to satisfy the specifications related to the possibility to perform fluid dynamical and optical measurements at the level of the aortic valve. As a consequence, the use of specific materials and components for the realization of the bench is necessary. In particular, in order to make optical measurements, flat and transparent plexiglass panels are needed to allow optical access. Furthermore, Magnetic Resonance Images can be obtained due to the absence of ferromagnetic materials. Particle Image Velocimetry (PIV) and Digital Image Correlation (DIC) measurements can be performed in order to know the velocity and deformation of the leaflets of the aortic valve.

The development of a test bench provided by anatomical components morphologically similar to the real one could help to obtain a consequent more realistic hemodynamic result.

For this reason, a closed hydraulic circuit, that simulates cardiac circulation, has been created exploiting the innovative additive manufacturing techniques. In order to make the characteristics of the simulation as similar as possible to the physiological ones, a Tomography Angiography of an adult woman, provided by Ospedali Riuniti di Ancona, has been used to obtain a left ventricle and an aorta morphologically correspondent to the real one. The material used to reproduce these anatomical components has elastic properties which allow the ventricle to contract and relax and the aorta to expand and recoil, as the real ones do.

Both the use of Tomography and the elasticity of the used material, allow to obtain more reliable results and give the possibility to reproduce the pathologies from which the patient is affected, simulating his clinical condition. In this way, each patient subjected to a surgical cardiac operation will have a valve adapt to his anatomical and physiological condition, reducing the post-operatory risks, including valvular rejection.

Furthermore, due to the presence of the aortic and left ventricle, the cardiac surgeon should have the possibility to perform a simulation of the operation directly on the test bench, before proceeding with the valve implant on the patient.

Moreover, the additive manufacturing techniques allow designing valves with malformation based on the pathology of the patient, in order to implant the prosthetic new valve reproducing exactly the current conditions.

In addition, due to the modularity of the bench, it is possible to modify individual parts of the circuit according to the desired objective.

1.1 Anatomy and Physiology of the heart and systemic circulation

The cardiovascular system is composed of a pump, the heart, several conduits of distribution and collection, the blood vessels, and a wide system of small vessels that

allow a rapid exchange between blood and tissues, the capillaries. The heart is composed of two atria and two ventricles: the atrium and ventricle of the left part constitute the left heart, atrium, and the ventricle of the right part compose the right heart. The circulatory system is divided into two parts: a pulmonary circulation, a loop through the lungs where blood is oxygenated and arrives at the left heart, and a systemic circulation, a loop through the rest of the body where oxygenated blood arrives at the tissues and then it returns to the right heart, as it is shown in figure 1 [1]. The heart can be considered a pressing-aspirant pump, with the function of applying the right pressure on a certain volume of blood, enabling the blood itself to be pushed into the blood vessels of the systemic circulation and to reach the tissues and the internal organs, allowing the maintenance of their specific vital functions.

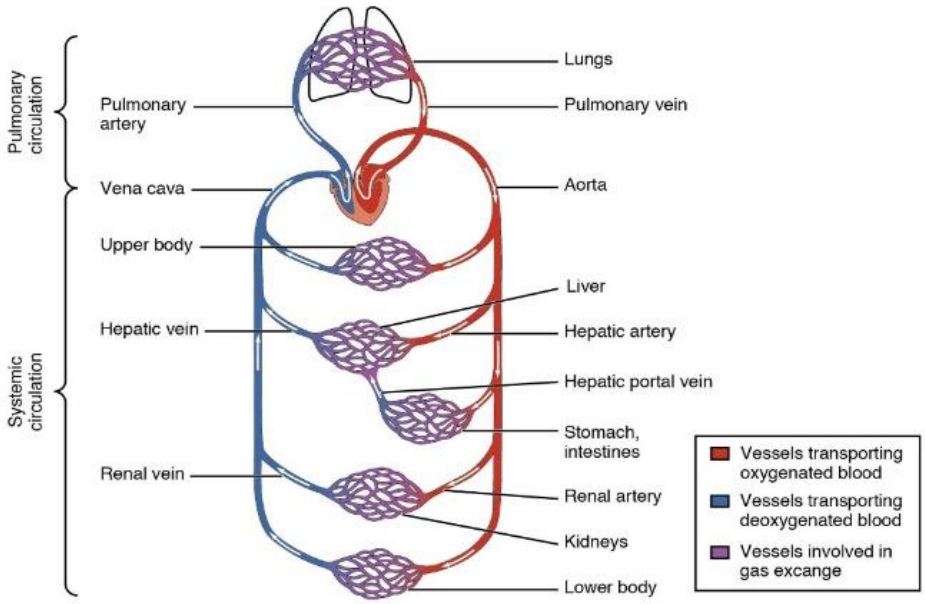


Figure 1. Schematic representation of systemic circulation and pulmonary circulation.

Atria receive the blood by the large veins and each of them transfers the blood in the underlying ventricle; ventricles push the blood into the two circulations, so the global cardiac functionality as the pump is dependent both on the proper operation of the left ventricle, which represents the major work performed by the heart and on the right ventricle. In order to regulate the flux of blood, four valves open and close with the

variation of pressure. As it is possible to notice in figure 2, two valves are located between the atrium and ventricle to prevent the reflux of blood into the atria when the ventricle contracts and two valves are positioned between the ventricle and large arteries to prevent the reflux of blood into the ventricles when they relax [2].

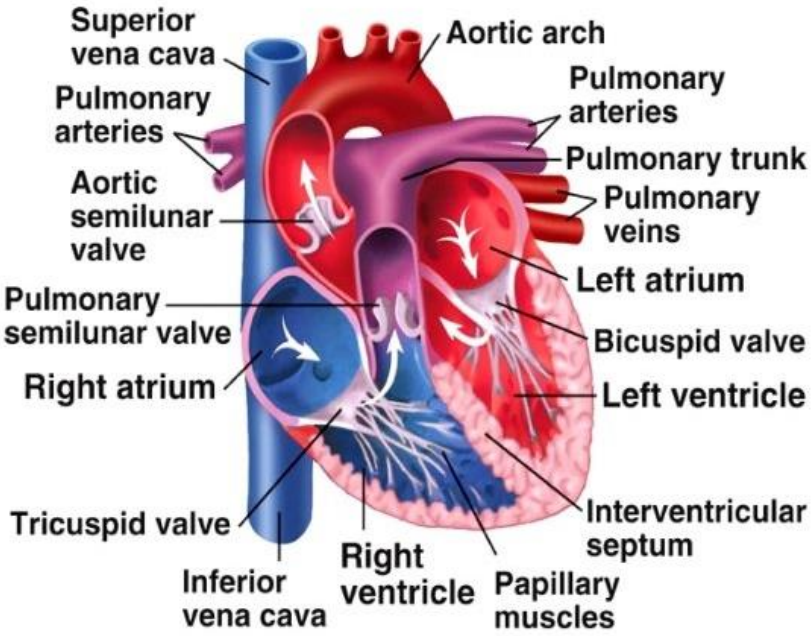


Figure 2. Cardiac district in its main components. The arrows indicate the path taken by the blood within the heart.

Left and right hearts work synchronously, so the contraction of the ventricles provokes the blood to be pushed both in the pulmonary circulation and in the systemic circulation. The right atrium receives the deoxygenated blood from the superior vena cava and the inferior vena cava, which collect all the blood coming from the superior and inferior parts of the body respectively. From the right atrium, initially, the blood passively flows toward the left ventricle through the tricuspid valve, and subsequently the atrium contracts and adds a small quantity of blood into the ventricle. The right ventricle contracts, causing the atrioventricular valve to close and push blood into the pulmonary artery, directed to the lungs. At this point, the capillaries are discharged of carbon dioxide and are charged with oxygen. The oxygenated blood flows toward the left atrium through the pulmonary veins and it

passively reaches the left ventricle, passing across the atrioventricular valve. As it occurs in the right part, the contraction of the left atrium causes the blood to be pushed into the ventricle. The left ventricle is constituted by powerful muscles, which allow a contraction able to push the blood into the systemic circuit. The increase of left ventricle pressure causes the bicuspid valve to close and the aortic valve to open [3].

It's important to notice that the valves passively open and close, depending on the pressure differences present on both sides of the valve.

The cardiac cycle can be seen as a succession of two phases: systole and diastole. Systole, also known as cardiac contraction, is the period during which muscles pass from a total relaxation state to their maximum mechanical activation and they push blood into the two circulations (pulmonary and systemic circulations). On the other hand, diastole, also identified as cardiac relaxation, is the period during which muscles relax, so from the state of maximum activation, they return to the resting state and the chambers fill with blood. As it is shown in figure 3, these phases alternate to make the flux unidirectional, and they are subdivided into:

1. **Passive ventricular filling**, where the filling of the ventricles takes place while the atrium and ventricle are relaxed;
2. **Active ventricular filling**, in which atria push an additional small amount of blood into the ventricles (about 25%);
3. **Isovolumic contraction**, which determines the closure of the atrioventricular valves, while the semilunar valves are still closed;
4. **Period of the ejection**, in which the ventricular pressure increases and exceeds the arterial pressure. The semilunar valves open and the ejection of the blood occurs;
5. **Period of isovolumic relaxation**, which causes a decrease in ventricular pressure so that the blood flows back toward the valve cusps and determines its closure.

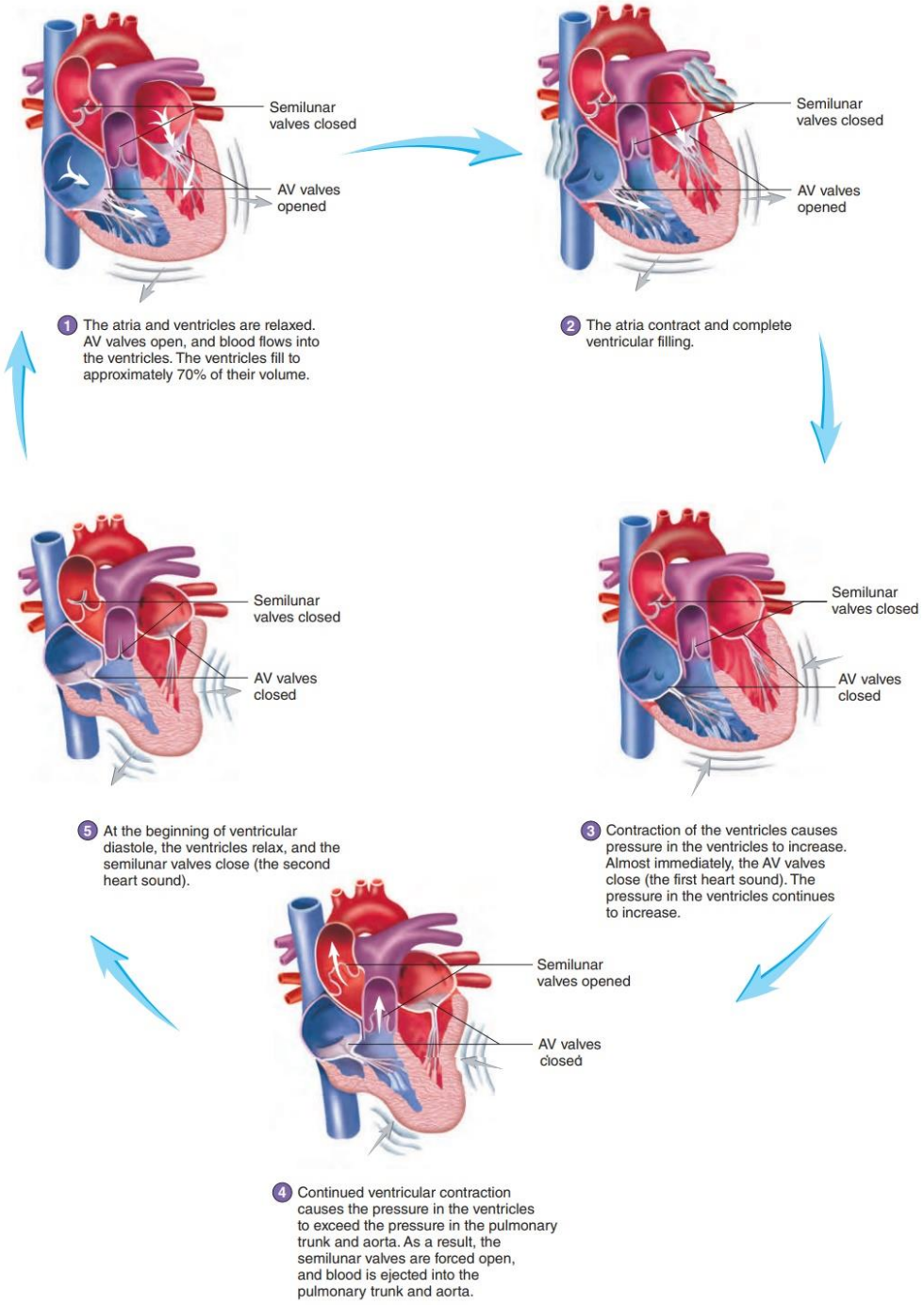


Figure 3. Five phases of the cardiac cycle with the description of the blood flow and the opening and closure of the valves.

The entire sequence of these phases constitutes a cardiac cycle, which normally has a duration of 0,8 seconds, which corresponds to a frequency rate of 75 beats per minute (bpm); it starts at the beginning of one heartbeat and ends at the beginning of another [4][5].

The main events of the cardiac cycle can be observed in the Wiggers diagram (figure 4): aortic pressure, left ventricular pressure, atrial pressure, left ventricular volume

and aortic flow, are represented in correspondence with the ECG signal. In particular, the curves that capture particular interest are the volume of the left ventricle which is included between 50 ml in the systolic phase, and 120 ml in the diastolic phase, the left ventricle pressure, which has a range of 5-120 mmHg, and finally, the arterial pressure which goes from 80 to 120 mmHg.

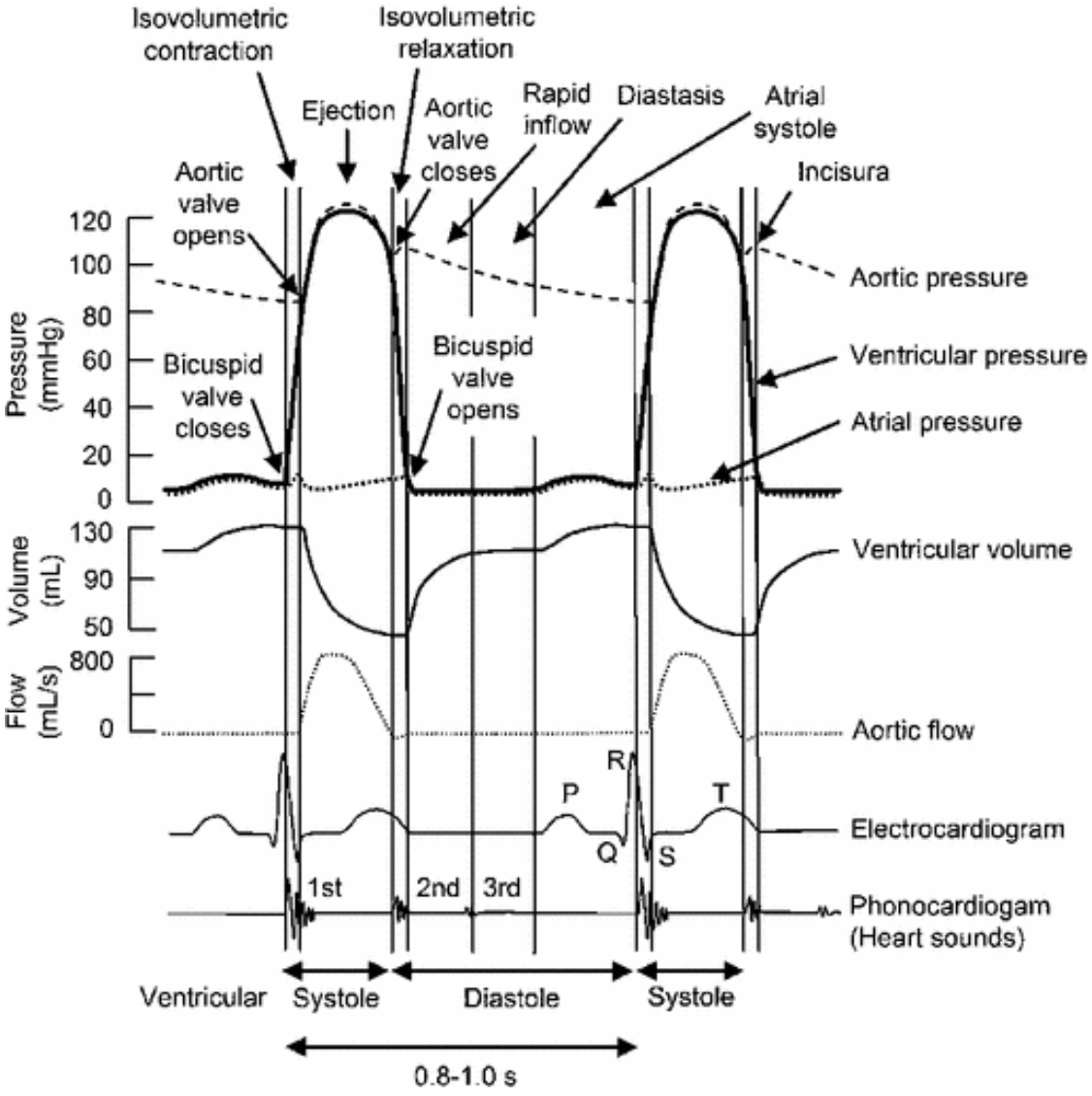


Figure 4. Wiggers diagram: aortic pressure, left ventricular pressure, left ventricular volume, aortic flow, electrocardiogram, and phonocardiogram.

Blood pressure decreases once the arteries branch, both due to the friction and because the volume of the blood is distributed in an increasing number of vessels of less caliber. Moreover, the elasticity of the larger vessels allows their distension when

the blood pressure rises during systole and their recoil during the diastole, making the blood flow more homogeneous than it would be in a rigid duct system. This phenomenon can be compared to the Windkessel effect. The arterial tree is represented by a tank, characterized by three quantities: pressure, volume, and compliance. The tank receives the blood from the aortic valve in a pulsatile manner and subsequently, it flows in the system formed by arterioles and capillaries, represented by a vascular resistance [6].

Among the four chambers that constitute the heart, only the left ventricle is under interest for this thesis work, since it's the part of the organ that will be reproduced. The left ventricle is constituted by thick walls of about 10 mm, to guarantee sufficient contrast to the resistance of the great systemic circulation. Its shape is slightly more elongated than the right ventricle and the two chambers are separated from each other by an intraventricular septum. The left ventricle is composed of an entrance area, which corresponds to the mitral valve, and an exit area, composed of the aortic valve. The mitral orifice has an oval outline, which measures 4-6 cm^2 with an average diameter of 32 mm; the aortic one has a circular outline of 22 mm, just near to the mitral valve and tilt of 50° concerning the latter one [7]. The mitral valve is constituted by two cusps: one placed forward and medially, called anterior cusp, and one located back and sideways, named posterior cusp. The aortic valve, instead, is formed by three cusps, divided into left, right, and posterior which are composed by a thickening of fibrous tissue, able to reach the complete closure of the valve. Opening and closing of the valves depending on the variation of pressure between the left atrium and ventricle, in the case of the mitral valve, and between the left ventricle and the aorta, as regards the aortic valve. In particular, as long as the pressure in the atrium is higher than that in the ventricle, the mitral valve remains open; when the ventricular pressure is higher than the atrial one, the valve closes, allowing the ventricle to push the blood into the aorta through the aortic valve. This latter one remains open until the ventricle pressure is higher than the aortic one, during the contraction phase. Several physiological parameters are important to understand if the

left ventricle works correctly. Some of these, to which we put particular attention to correctly reproduce the behavior of the left ventricle, is the stroke volume (SV) and the Cardiac Output (CO), which are the whole quantity of blood pushed by the ventricle in systole and the volume blood which the left ventricle can eject in a minute, respectively. In particular, SV increases as the force of contraction of the ventricle itself increases, and in a healthy subject, its value is 70 ml. CO is fundamental to evaluate how the heart efficiently responds to the body's demands of blood to maintain adequate tissue perfusion and its average value in an adult healthy man is 5 l/min.

1.2 Cardiac prosthetic valves

The cardiac valves can be affected by various pathologies, leading to hemodynamic malfunctions. The two most common valvular diseases are stenosis and regurgitation. Stenosis is the shrinkage of the valvular orifice and it constitutes an obstruction to the blood flow. Regurgitation represents the inability of the valve to completely close, allowing the blood to flow back.

Aortic stenosis is an obstruction to the passage of blood flow from the left ventricle to the aorta (figure 5). It is one of the main diseases and it causes the left ventricle to make a greater effort to push the necessary blood into the aorta. As consequence, the left ventricle is subjected to a thickening of its muscular wall (left ventricular hypertrophy) and then to a weakening of its contractile power.

Treatment of aortic stenosis varies according to the severity of the valve narrowing. If the pathology is not severe and causes no symptoms, the specialist performs periodic monitoring of the condition through echocardiography. If instead, aortic stenosis is severe, surgical therapy is essential. There are different intervention techniques:

-replacement of the aortic valve: it consists of removing the original aortic valve and replacing it with a new, artificial, or biological valve. This is an operation that

can be performed either through thoracotomy or through transcatheter modality, which is less invasive;

-repair of the aortic valve: it involves the remodeling of the aortic valve to restore its original functions. Most of the time it is performed through a thoracotomy, but sometimes it is necessary to practice less invasive methods (mini-thoracotomy or transcatheter modality);

-balloon catheter valvuloplasty: it consists in enlarging the valve orifice by passing a catheter through the aortic valve. Unfortunately, this approach has temporary effects and it is indicated only in very young patients.

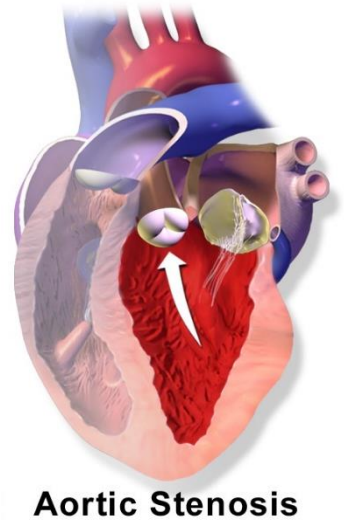


Figure 5. Stenosis of the aortic valve.

Aortic insufficiency, or aortic regurgitation, is a pathology characterized by the failure in the hermetical closing of the aortic valve and the consequent reflux of blood from the aorta to the left ventricle (figure 6).

Treatment of aortic regurgitation varies according to the severity of the blood regurgitation itself. If the aortic insufficiency is not severe, periodic monitoring of the condition is performed. On the other hand, if the pathology is severe and produces

important symptoms, surgical therapies, such as replacement or repair of the aortic valve, are necessary.

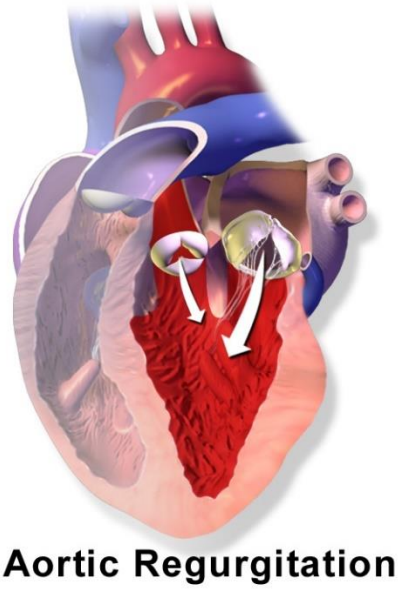


Figure 6. Regurgitation of the aortic valve.

When the valves undergo calcification and degradation processes they may no longer be able to open easily and this condition can lead to the just mentioned pathologies. The consequence is that the heart muscle will have more difficulty in pushing the blood through the valves, resulting in a situation of chronic suffering of the organ and pressure overloads. The main symptoms of this condition are excessive weakness, difficulty in breathing due to gradually decreasing efforts (dyspnoea), fainting, chest pains, and cardiac arrests. Unfortunately, when valve stenosis becomes severe, a serious condition of disease can lead to death. For this reason, it is advisable to intervene with treatment or prosthetic replacements of the native valves.

The prosthetic cardiac valves (PHV) are implanted when a pharmacologic treatment or a constructive surgical intervention is not sufficient to restore the correct operation of native valves. However, risk factors must be considered: old age, body surface, sexuality, condition of the left ventricle, presence of other heart diseases.

PHV can be divided into two classes: mechanical valves, which are completely made in synthetic materials, and biological valves, composed of biological tissues (porcine,

bovine, and human). For each of them, there are advantages and disadvantages. The mechanical valves have a longer life duration than the biological ones. They can correctly work for 20-30 years, but they require a permanent anticoagulant treatment. On the contrary, the biological ones, don't require specific treatment but they are subject to deterioration and they are implanted on elderly people.
The most important characteristics that a prosthetic valve should have are:

- sterility
- non-toxicity
- durability
- appropriateness to be implanted in the heart
- minimal resistance to flow
- resistance to mechanical and structural wear
- suitability for the cardiac structure
- minimal regurgitation when the valve is closed
- low probability of causing thromboembolic complications
- minimal damage to endothelial tissues of the cardiovascular structure and blood components
- no noisiness
- visibility by radiography
- acceptable cost.

The mechanical prosthetic valves are divided into three different components: the housing, the sewing ring, and the occluder. The housing is a metallic structure that allows the occluder to move, regulating the blood flow. The sewing ring is the fundamental component through which the prosthesis joins the surrounding tissue. The occlusion is the movable part of the mechanical prosthesis: it opens and closes depending on the pressure differences.

The **caged-ball** was the first implanted artificial valve, in 1951 from Dr. Charles Hufnagel and it was used to treat aortic insufficiency (figure 7).

Figure 7. Caged-ball valve model of Hufnagel.

Specifically, a polyethylene occludent ball was contained in a Plexiglas cage and the structure was inserted into the descending aorta. After the implantation, the blood no longer flowed centrally, but to the sides of the ball, causing a peripheral flow.

The most serious consequences associated with cardiac valve implantation are thrombosis, bleeding, tissue overgrowth, infections, valve failure caused by material fatigue, and chemical modifications.

The use of the caged-ball valve, in 1960 was substituted by the **Starr-Edward ball-and-cage** valve (figure 8), projected to be inserted into the native diseased valve position. This technique was used both for mitral and aortic valve substitution.

Figure 8. Ball-and-cage valve realized by Starr-Edward

During the years, the Starr-Edward ball-and-cage valve has undergone several changes, mainly concentrated on the materials and the construction techniques keeping unchanged the operating principle of the valve. Moreover, other models of caged-ball valves have been designed: among them, we put particular attention on the **Smeloff-Cutter** valve (figure 9), composed of a cage, which holds the ball into a closed position; a small space around the ball guarantees the flow to pass easily, also

due to the smaller dimension of the ball. This space produces reflux, which may prevent thrombotic events.

Figure 9. Ball-and-Cage model of Smeloff-Cutter.

Another ball-and-cage valve was the **Magovern** (figure 10), composed of two rows of mechanical teeth, wedged around the orifice of the ring. This valve has not been used anymore because it took the wrong position in the calcified ring.

Figure 10. Ball-and-Cage valve model of Magovern.

In 1965 and 1967 **Kay-Shiley** and **Beall** valves were introduced as mitral valves, but due to their poor hemodynamic characteristics, they are not widely used. Afterward, a valve with better features than the previously designed valves was employed: the **tilting-disc** valve, composed of a single oscillating disc of polymeric material. Subsequently, **Bjork-Shiley** and **Lillehei-Kaster** valves (figure 11 and 12) were the first models with a free mobile disc.

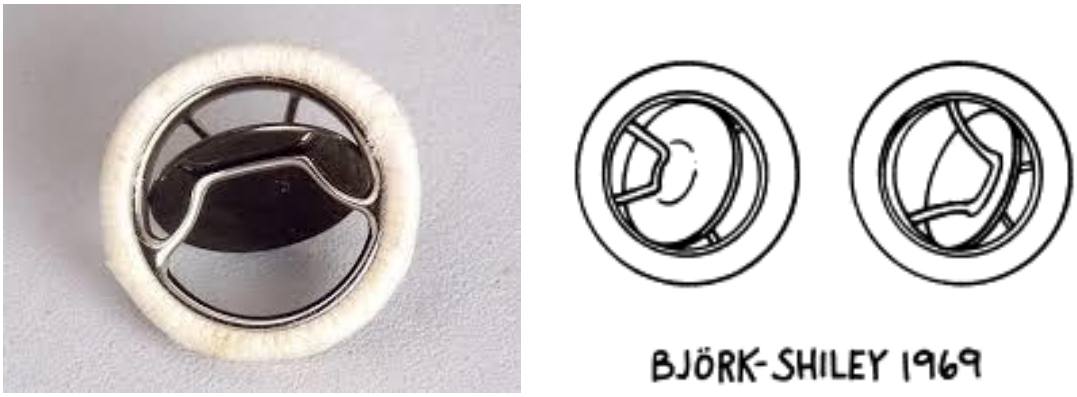


Figure 11. Tilt-disc valve model of Bjork-Shiley.

Figure 12. Tilt-disc valve model of Lillehei-Kaster.

In these valves, the innovation consists in the reduction of blood flow distortion, compared to the caged-ball, through the rotation of a circular occluder, which allows the blood to flow with greater regularity. Bjork-Shiley valve has a smaller thickness than the caged-ball one, so it's easier to place it into the narrowest anatomical sites, without damaging the surrounding tissues. Moreover, the occluder was realized in Delrin, a biocompatible material, with low thrombotic risk, but then, it was substituted with carbon due to its low friction coefficient and its high durability. In 1976 the **Medtronic-Hall** valve was introduced, characterized by a centrally hinged occluder and by a titanium housing covered with pyrolytic carbon (figure 13). This structure can hold the disc, to control its opening angle and it allows the disc to move

downward, improving the velocity of the flux between the orifice of the ring and the edge of the disc.

Figure 13. Tilt-disc Medtronic Hall model

In 1984, the **Omniscience** valve (figure 14) was created as an evolution of the Lillehei-Kaster model.

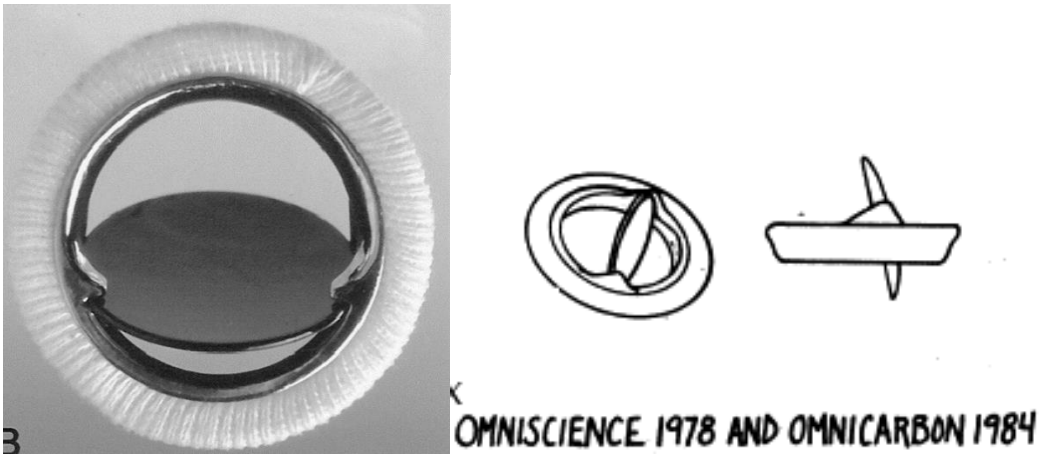


Figure 14. Tilt-disc valve Omniscience model.

In 1977 in addition to the Medtronic-Hall valve, the first bileaflet valve was realized by St. Jude Medical (figure 15). It was characterized by two semi-discs, which act as occluders and can open and close based on blood pressure, making the flux very similar to the physiological one. It has an excellent hemodynamic characteristic, e.g.

the centrality of the flux, the regurgitation which avoids the thrombus formation, the reduction of the transvalvular pressure jump, the long duration, the biocompatibility.

Figure 15. Bileaflet valve model realized by St. Jude.

The most used bileaflet valves are:

St. Jude Medical Regent: higher than the original bileaflet, it allows the passage of a greater flow and a greater structural strengthening of the housing, which is an important characteristic for the increasing of the orifice area available for flow (figure 16).

Figure 16. St. Jude Medical Regent valve model.

Sorin Bicarbon: the curvature of the two valve flaps, reduces the pressure loss caused by the central orifice of the original bileaflet. Since the pivots are constituted by two spherical surfaces with different radii of curvature, the wear times are reduced because the flaps rotate throughout the housing (figure 17).

Figure 17. Sorin Bicarbon valve model.

ATS Open Pivot: it reverses the mechanism of the pivot, exposing it to the high-velocity flux. It allows the removal of the cells placed on the surface of the pivot, avoiding thrombus formation (figure 18).

Figure 18. ATS Open Pivot valve model.

On-X: it has a close-ratio among length and diameter and its flaps open of 90° to the valve body. This leads to an improvement in blood flow (figure 19).

Currently, the most implanted valves are the mechanical ones, in particular, the bileaflet model is the most convenient.

Figure 19. On-X valve model.

The biological prosthetic cardiac valves (figure 20) are composed of three flaps, capable of deforming due to pressure change. The valves can be divided into three classes: homologous, autologous, and heterologous.

The **homologous** valves are obtained by human corpses; they are sterilized and subsequently implanted instead of the diseased valve. In the open position, these

valves allow a central flow and react to the deformations based on the surrounding anatomical site. A disadvantage is represented by the fact that the tissues are no longer alive, and so they are devoid of cell regeneration activity. Consequently, they are subject to wear for a long time.

The **autologous** valves are taken directly from the tissues of the patient. The valve can be substituted with the pulmonary valve, or with an autologous fascia lata (a membrane that wraps the thigh muscle), but this method is not widespread due to the inadequate mechanical response in a long time.

The **heterologous** valves are made from animal tissue, treated with chemicals to prevent an antigenic response. Initially, it was treated with formaldehyde, but the stiffness of the tissue was noticed; subsequently, they were treated with glyceraldehyde due to the capability to decelerate the degenerative processes and to the presence of collagen, able to provide flexibility and to decelerate the antigenicity of the transplanted tissues. The calcification of the flaps causes valvular insufficiency in younger people.

Moreover, the glyceraldehyde was associated with cytotoxicity, inflammatory response, and calcification.

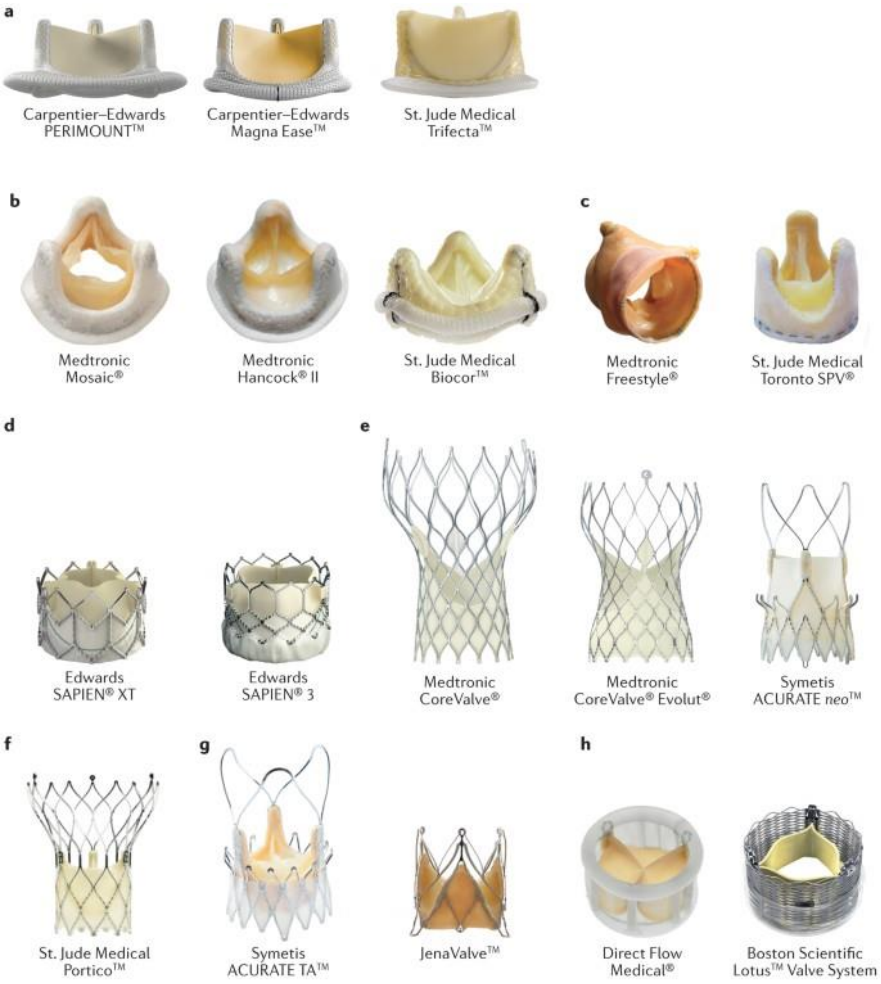


Figure 20. Types of surgical and transcatheter aortic valves. A) Stented pericardial bovine surgical aortic valve bioprostheses. B) Stented porcine surgical aortic valve bioprostheses. C) Stentless surgical aortic valve bioprostheses. D) Balloon-expandable bovine pericardial tissue transcatheter bioprostheses. E) Self-expanding porcine pericardial tissue transcatheter bioprostheses. F) Self-expanding bovine pericardial tissue transcatheter bioprosthesis. G) Self-expanding native porcine leaflets transcatheter bioprostheses. H) Alternative expansion design bovine pericardial tissue transcatheter bioprostheses.

The most important advantage of the mechanical valve is its unlimited durability. They are realized with biomaterials such as pyrolytic carbon and titanium. The disadvantage is represented by the necessity to use anticoagulant therapies to avoid thrombolytic events. Unfortunately, these therapies require continuous monitoring of the patient and hemorrhagic processes. The mechanical valve implantation is applied on younger people and patients who already have an implanted mechanical prosthesis.

The higher advantage of the biological valves is the lower probability to have thrombolytic events concerning the mechanical ones. In fact, with this type of valve,

anticoagulant therapy lasts a few months. The disadvantage is the fatigue of the material, the wear of the flaps, and their calcification.

The biological valves fail typically after 10-15 years after implantation and they need to be substituted.
The mechanical valves require anticoagulant therapy since they are thrombogenic. Based on this consideration, the mechanical valves are preferred for younger patients, instead, the biological valves are used for elder patients.

1.3 Transcatheter aortic valve implantation and Valve-in-Valve

Transcatheter aortic valve implantation (TAVI) is a technique applied in medicine if the traditional surgery, which involves the opening of the chest and extracorporeal circulation, cannot be executed. TAVI is a minimally invasive procedure through which it's possible to apply valve prostheses in case of aortic valve stenosis without having to stop the activity of the heart. This technique is preferred in case of delicate cardiovascular health, additional pathologies, and advanced age that preclude the classic approach. According to the patient's conditions and the indication of the cardiologist, the surgeon, and the anesthetist, the intervention can take place in two different ways: through an incision of the chest of 4-5 centimeters at the level of the intercostal space (**Transapical TAVI**) or the introduction of catheters, used for the releasing of the prosthesis, inserted directly from the femoral artery (**Transfemoral TAVI**) [8][9]. In particular, the transfemoral TAVI consists of the insertion of a preformed prosthetic valve via catheter, through a femoral artery (figure 21). The valve directly replaces the malfunctioning native valve and guarantees the patient a faster and less difficult rehabilitation.

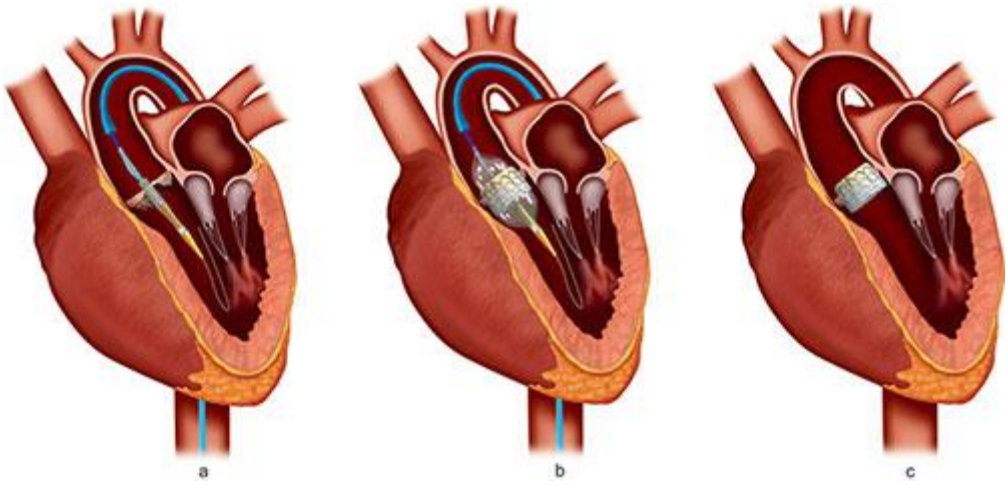


Figure 21. Transcatheter aortic valve replacement a) crimped valve placed across the aortic annulus; b) Valve expansion; c) Valve post-deployment

On the other side, transapical TAVI is used by cardiac surgeons as an alternative to transfemoral one when obstructive diseases of the peripheral arteries are present. This approach is used also to treat the degenerated biological prosthesis, both aortic and mitral. In fact, due to the limited durability of the biological valves, a replacement of the prosthesis itself is required and a reoperation performed with conventional surgical technique has a fairly high risk. Therefore, it's possible to implant a new biological valve inside the degenerated prosthesis (Valve-in-Valve procedure).

Despite the enormous advances made in the medical field in recent years, operative complication exists and will never be completely eradicable. It is natural that the more complex the clinical situation of the patient, the easier it is to incur undesirable consequences. In particular, the predisposition to certain anatomical conditions plays an important role in the risks of cardiovascular surgery, such as severe diffuse or asymmetrical calcifications, vascular aneurysms, cardiac conduction disorders, advanced arteriosclerosis, congenital valvular bicuspid, severe ventricular dysfunction previous use of stent-less / supra-annular bioprostheses. There is also the possibility that the normal electrical conduction pathways of the heart are influenced by the position of the prosthetic valve, determining the need for a definitive Pacemaker implant. Moreover, rarer complications are the rupture of the aortic ring,

malposition, embolization of the positioned prosthesis, the perforation of the left ventricle or the vascular structures [10].

Transcatheter correction of degenerated cardiac surgical aortic bioprosthesis (Valve-in-Valve (ViV)) represents a feasible and less invasive therapeutic option than the cardiac surgery reoperation. The use of ViV for the treatment of high-risk patients with degenerated aortic bioprostheses is associated with relatively low mortality, with an improvement in hemodynamic parameters, and with excellent evolution of the functional capacity and quality of life at 1 year [11].
However, the risk for patients subjected to a ViV TAVI to have a patient-prosthesis mismatch needs to be considered. Since the transcatheter heart valve (THV) is implanted within the ring of the existing bioprosthetic valve fracture, it's difficult to find the right prosthesis because the expansion and the achievable orifice area of the THV are limited [12]. A possible solution for this problem could be the use of a THV with supra-annular leaflet positioning, in order to obtain a larger effective orifice area due to the position of the prosthetic leaflets [12].
One of the most important risks for ViV TAVI is coronary artery obstruction which depends on several factors: low coronary artery Ostia, narrow coronary sinuses, bulky bioprosthetic leaflets, reimplanted coronary arteries. Another consideration before a ViV TAVI needs to be done: a careful selection of the type of THV is necessary to avoid post-procedural risks. Although both self-expanding and balloon-expandable THVs are approved for use in ViV TAVI, the first ones present a superior procedural hemodynamic and increased effective orifice area, due to the supra-annular position of the prosthetic leaflets on the self-expanding frame [13].

1.4 State of the art of test benches for transcatheter aortic valves

In order to perform some tests to verify the correct functioning of transcatheter aortic valves, a hydraulic circuit is necessary. For this reason, several test benches which

simulate the systemic circulation have been created until now. In particular, a pulsatile system driven by motors able to recreate an artificial heartbeat has been used. Early easier systems consisted of a chamber from which a steady flux comes out and it had a resistance capable of providing a jump of pressure. New development instead, includes specific physiological characteristics such as accurate pulsatile flow, resistances, compliances, and contraction of the atrium. Many of these systems include transparent ventricles of flexible material for visualization of the flow to the level of the valve.

Now, a brief review of some articles regarding the use of a test bench will be done in order to introduce the argument and to understand which are the starting points for the design of a test bench.

Knott et al. (1988) [14] compared several types of mechanical aortic heart valve prostheses through the use of pulse duplicators. In order to obtain a nonstationary flow of the blood similar to the physiological one, adjustable compliances and resistances have been used; the left ventricle has been mimed by a silicone-made flexible ventricular sac and its volume displacement has been achieved by an electrohydraulic drive unit; the piston expanded or contracted the ventricle using a compression fluid and an air volume has been introduced in the ventricle chamber to simulate the variable ventricular compliance [14]. Piezoelectric catheter-tip pressure transducers have been used to measure pressure in the left atrium, in the apex region of the left ventricle, and the ascending aorta; two electromagnetic flowmeters, located 8 diameters downstream of the aortic valve and 1,5 diameters upstream of the mitral valve, have been used to record the flow [14].

Moreover, the work of **De Paulis R. et al.** (2005) [15] had the aim to determine whether the presence of vortices inside the sinus immediately above the prosthetic aortic valve could negatively influence the hydrodynamic in vitro performances of a prosthetic heart valve. They used a specific design of the pulse duplicator to test several aortic prosthetic valves. Adjustable compliances and resistances have been used to simulate the physiologic input and output impedances of the left circulatory

system; the silicon ventricle and the aortic valves conduit have been realized following the physiological geometry; an electrohydraulic drive unit has been used to generate the volume displacement of the left ventricle; a piston has been employed to expand and contract the flexible model ventricle through a fluid inside the compression chamber. Regarding the determination of pressure, volume and flow signals, they have been measured at several positions within the pulse duplicator. In particular, pressures have been recorded by a gauge pressure transducer within the atrium, in the apex region of the ventricle, and the ascending aorta; instead, the flow has been recorded by an electromagnetic flowmeter, located upstream of the mitral valve and 4 diameters downstream of the aortic valve [15].

Furthermore, **Querzoli et al.** (2014) [16] investigated through an electromagnetic flowmeter the fluid dynamic modifications occurring as a consequence of the morphological changes induced in the aortic root by Marfan syndrome. They utilized the pulse duplicator to observe the differences between a healthy aortic root and a pathological one. The aortic root was made of silicon rubber and it was positioned inside an aortic chamber with Plexiglas walls, filled with water; two sensors of pressure were located upstream of the mitral valve and 6,5 diameters downstream of the aortic valve; an electromagnetic flowmeter was situated just upstream from the aortic valve. The aortic chamber was connected to a vertical tube, whose extremity was in communication with the atmosphere, and two resistances, together with the compliance, simulated the impedance of the systemic circulation [16].

Querzoli et al. (2016) [17] in another study, observed the flow in the aortic root, including the coronary arteries in the model of the pulse duplicator. Specifically, they used a ventricle made by rubber silicon located in a closed ventricle chamber, filled with water, whose movement was controlled by a piston driven by a linear motor: the changes of volume of the ventricle corresponded to the stroke volume of the piston. As regards the valves, a hydraulic check valve has been positioned in the mitral position and a prosthetic bi-leaflet mechanical valve has been utilized as an aortic valve. The aorta has been made of silicon rubber and it has been located into an aortic

chamber, filled with water, and connected to a vertical tube in contact with the atmosphere to control the distensibility of the aorta; when the fluid flowed through the resistance, the diameter of the aorta increased. Other two resistances and two compliances reproduced the impedance of the systemic circulation, including the coronary arteries. Two piezoelectric sensors have positioned upstream of the mitral valve and 6,5 diameters downstream of the aortic valve to measure the pressure and an electromagnetic flowmeter was used to record the flow rates [17].

Additionally, **Bazan et al.** (2016) [18] tested prosthetic heart valves by using a simplified model of the cardiac simulator but maintaining the left ventricle morphology and the flow characteristics similar to the human heart system. The physiological parameters have been taken into account to reproduce the rest condition as closer to reality as possible (e.g. heart rate, end-diastolic volume, ventricular stroke volume, left ventricular pressure, and aortic pressure). Two invasive pressure transducers, an electromagnetic flowmeter, and a temperature control system have been the instruments included in the cardiac simulator. The left ventricle has been made by a silicon membrane, to allow the contraction and relaxation, and an optical platform has been used to enable the use of some techniques for optical measurements; a linear slide table has been used to convert the rotational motion of the motor into a linear displacement of a piston, connected to the ventricle chamber to induce volumetric changes of the fluid; a characteristic resistance, adjustable compliance, and an adjustable peripheral resistance have been the 3 elements of the Windkessel model used to modify the discontinuous flux of the cardiac output [18].

Furthermore, **Feng et al.** (2016) [19] performed some tests on the transcatheter aortic valves and evaluated the importance of the thickness of the leaflet tissue using a pulse duplicator system to simulate the physiological conditions of the left heart. The system was composed by resistance and compliance to reproduce at Windkessel model; two pressure probes and an electromagnetic flowmeter were used to measure flow rate and pressure in front and back of the valve; the transcatheter aortic valves

with different thicknesses were transported into the position of the silicone aortic annulus and they were tested in normal saline fluid, heated to 37 °C [19].

2. Materials and Methods

The creation of a closed hydraulic circuit is necessary to simulate the systemic circulation and to perform tests for the study of the heart valve's behavior. It is also useful to monitor how the performance of the cardiac prostheses can be influenced by hemodynamic parameters, such as the cardiac output or the blood pressure.

As was described in the first chapter of this thesis, the first versions of the closed hydraulic circuits were made to test mechanical valves. Subsequently, more recent test benches were composed of pulsatile systems driven by motors able to recreate an artificial heartbeat and the inertia of the human body was simulated by including compliances and resistances into the circuit.

Starting from these assumptions, the present thesis work has the aim to design and develop a modern test bench for ViV TAVI. It could be used by cardiologists to observe and study the behavior and the adaptability of a cardiac valve before the surgical operation. Huge benefits can be exploited from a simulation of the pathologies, the physiological and the hemodynamical parameters, and, possibly, of the operation itself. In the specific case of the ViV TAVI, it is possible to analyse the hemodynamic characteristic of the valves in order to understand if the patient and his current pathologies are compatible with the prosthesis. In order to make the organ as close as possible to human physiology, additive manufacturing techniques have been involved in the reproduction of the left ventricle and the aorta. So there could be the possibility to mimic pathologies related to the organ, to the blood vessel, or to the valve itself through the use of suitable materials. Another important aspect is related to the reproduction of the pulsatility of blood flow, which depends on the actuator. It should be able to control the membrane of a pump, from which the volume of water pushed and pulled in the ventricular chamber will depend. In order to properly control the movement of the membrane, the actuator should be equipped with a potentiometer, which can provide a feedback position during the variation of its resistance. Moreover, in order to perform optical measurements on the cardiac

prosthetic valves, transparent and flat surfaces are needed around the ventricle to guarantee optical access from two different directions for the stereovision. The bench should also allow testing of different types of valves by inserting them in the appropriate place between the left ventricle and the aortic arch. The precise position of the valve can also change according to the need and the comorbidities of the patient to decrease the post-operative risks due to the reduced movement of the leaflets. The a priori knowledge of the position and the malformation of the cardiac valve could help the surgeon in the simulation of the surgical operation itself, through the precise reproduction of the clinical condition of the patient.

To summarize, the design of a proper test bench should satisfy the following requirements:

- Customized heart
- Different types of valves that can be tested
- Access for optical measurements
- Aorta in compliance chamber
- Modularity
- Simulation of each kind of left ventricular and aortic disease
- Possibility to place the valve in different positions
- Potentiometer included into the actuator
- Simulation of aortic valve malformation
- Possibility to do practice on the bench for the surgeon

2.1 Concept design of the bench

Note the goals and the characteristic of the project, a translation of the essential components of the system into dimensional terms was made. The physical device can be simplified into a closed hydraulic circuit of pressure pipelines consisting of a series of tubes, tanks, valves, and resistances located in precise positions.

Particular attention has been put on the reproduction of physiological dimensions and elastic characteristics of the left ventricle and the aorta. For this reason, Thoracic Tomography Angiography has been indispensable to size and rebuild the right morphology of the two components. This approach allows to perform a study about any kind of pathology related to the aortic arc and left ventricle because it is possible to exactly reproduce the organ of the patient before the surgical operation. From the Tomography, directly a 3D solid has been obtained through the use of CAD programs. The additive manufacturing techniques played a fundamental role in the development of the present work because major freedom of choice has been allowed in the realization phase. In particular, as regards the ventricle and the aorta, different kinds of material and thickness of the walls can be utilized in order to find the right coupling to obtain the correct elastic characteristics able to mimic the contraction and the relaxation motion. Another important application of the 3D printer has been the customized realization of the support for the pump, but also of some connection components between the simulated heart and the chambers of the hydraulic circuit. Moreover, in addition to the mechanical valve provided by Ospedali Riuniti di Ancona, a 3D-designed valve has been printed with silicon material in order to try several kinds of the valve on the test bench and to demonstrate that there is the possibility to reproduce valves with specific diseases. An advantage in the use of the additive manufacturing techniques has been the possibility to choose the specific place of the valve as soon as possible to the real one but also considering the possibility to have problems in the aperture and closure of the leaflets helping the surgeon to understand which can be the risks in a post-operative condition.

Underlined the available tools, presently all the followed steps for the realization of the bench will be described in detail.

2.2 Applicable measurements techniques on the test bench

The characteristics of the present test bench take into account the possible measurements which could be done both on the fluid and the aortic valve.

In particular, the **Particle Image Velocimetry (PVI) technique** can be performed on the flux, the turbulence, and the microfluidic events which occur at the aortic valve level. PIV is an optical method of flow measurement and it is used to assess the instantaneous velocity of the fluid following the particles seeded into the fluid, able to follow the flow dynamics. The particles are illuminated so that they are visible and their motion is used to calculate speed and direction.

Another optical measurement technique is the **Digital Image Correlation (DIC)**, which employs image registration techniques for accurate 2D and 3D measurements of shape, displacement, and deformation of solid surfaces. The solid surface is "speckled" in order to define targets on the surface and those targets are observed in a detailed way by a couple of digital cameras; digital image correlation among images coming from each camera provides the local displacement. 3D deformation of the material can be assessed.

As regards medical measurement, **Magnetic Resonance Imaging (MRI)** can be used to form images of anatomy and physiological processes of the body, through specific scanners which use a strong magnetic field and radio waves. In particular, in the cardiac field, it is used to measure the structure and function of the heart exploiting the high tissue contrast between myocardium and blood [20].

Classical **pressure measurements techniques** can be used to measure pressure into the ventricle and the aortic arc through the use of pressure sensors, which are provided of a membrane able to deform when pressure is applied on it and, due to the presence of a Wheatstone bridge, the deformation produces electric resistance changes, proportional to the pressure.

Electromagnetic flowmeters, instead, can be used to measure the flow at the aortic valve level. It is based on the principle of electromagnetic induction: the fluid flow is measured by the voltage induced across the liquid by its flow through a magnetic field, which is applied to a tube. The potential difference is proportional to the flow velocity perpendicular to the flux lines.

All the parameters coming from the previously described measurement techniques are useful to help the surgeon to simulate a cardiac operation before implanting the valve directly on the patient. It allows to previously evaluate the post-operatory risks and to select the most suitable valve based on the cardiac condition of the patient.

2.3 From physiological parameters to the preliminary design of the bench

Since control of the pulsatile flow is needed in order to correctly reproduce the heartbeat, an actuator able to lower and raise the membrane of the pump is required. To find the right actuator, a careful analysis of the available parameters has been done: first of all, instantaneous pressure and volume of the left ventricle and instantaneous arterial pressure were found to be indispensable as starting points for the subsequent calculation of physiological parameters (figure 22, 23 and 24).

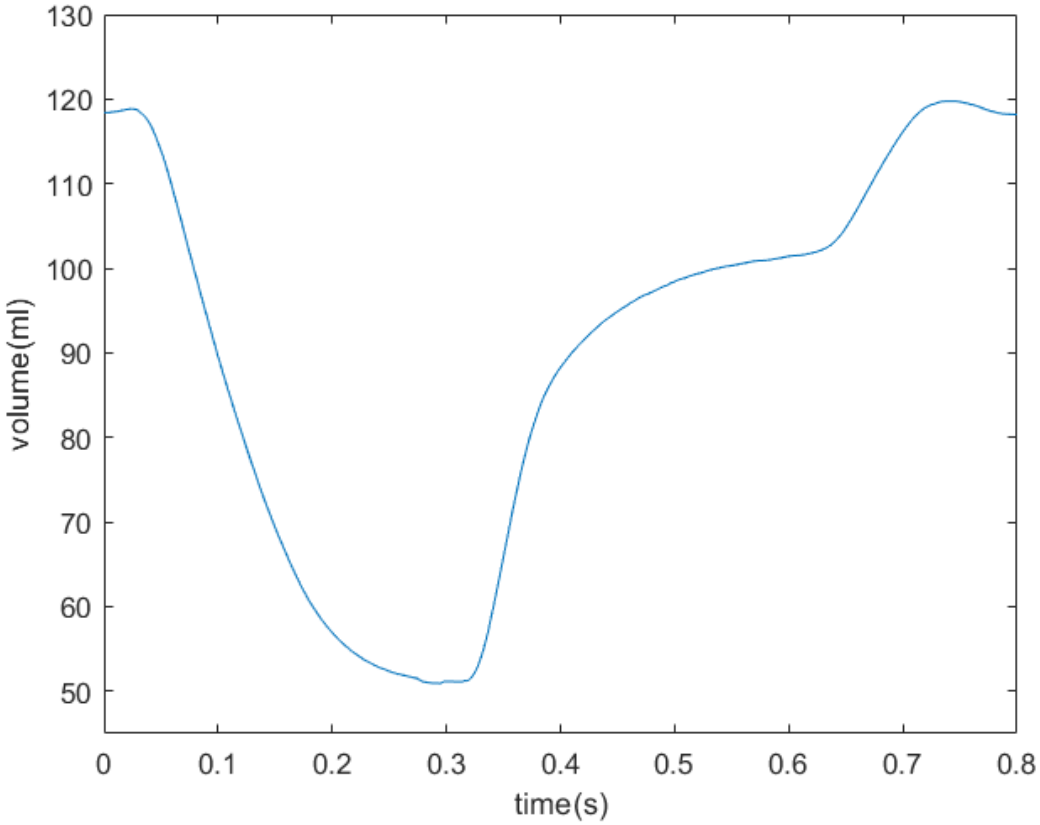


Figure 22. The physiological curve of left ventricular volume in a cardiac cycle.

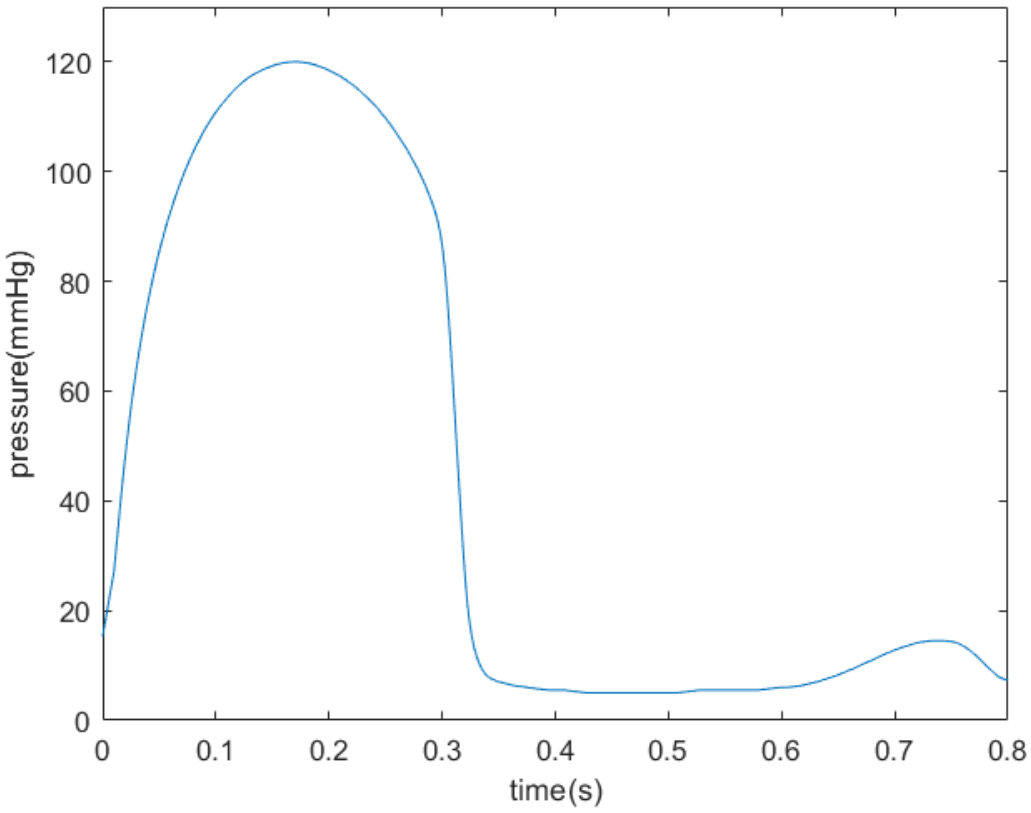


Figure 23. The physiological curve of left ventricular pressure in a cardiac cycle.

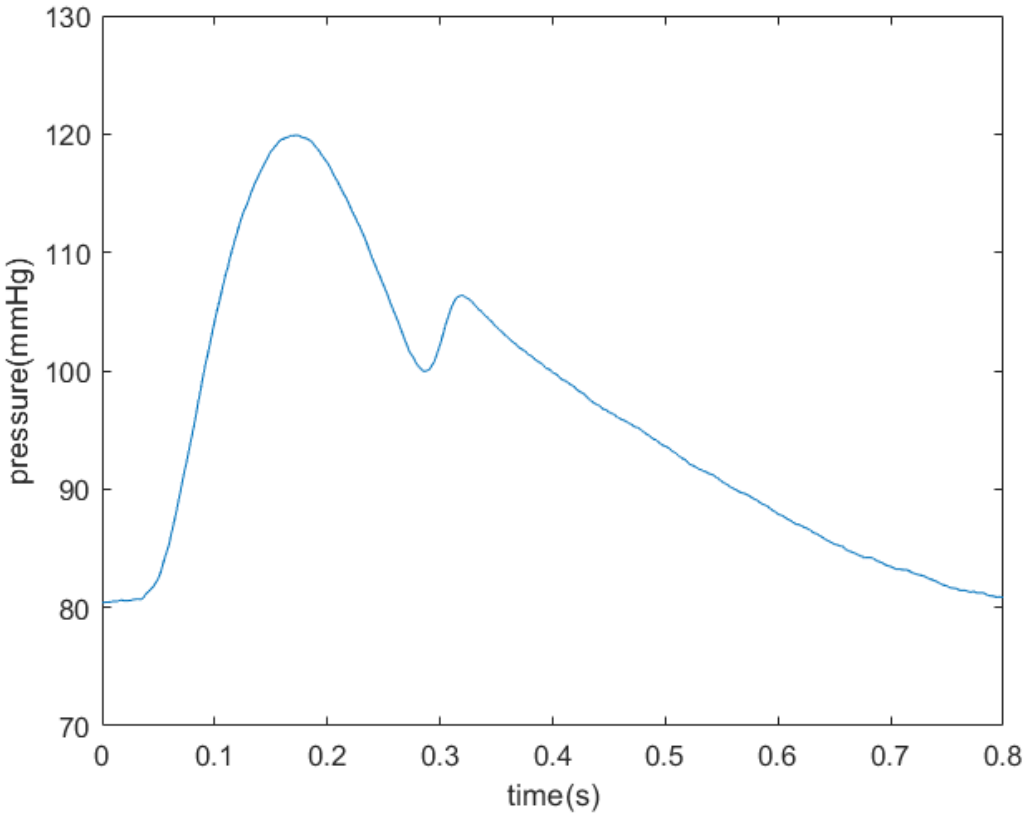


Figure 24. The physiological curve of arterial pressure in a cardiac cycle.

The previously mentioned curves that have been obtained from the code are present in the attachment.

From these curves, SV and CO have been found: as it can be seen in equation 1, SV has been calculated by subtracting the volume of blood that remains in the ventricle after systole (end-systolic volume) from the volume of blood present just before the systole (end-diastolic volume) and its value is 70 ml. CO, instead, is calculated by multiplying the Heart Rate and the SV and its average value is 5,16 l/min (equation 2). Both results are consistent with the physiological values of a healthy adult person. Matlab code passages are listed in the attachment.

$$stroke\ volume = end\ diastolic\ ventricle - end\ systolic\ ventricle \quad (1)$$

$$cardiac\ output = heart\ rate * stroke\ volume \quad (2)$$

2.4 Realization of test bench

The previously observed curves played a fundamental role during the identification phase of an appropriate actuator, able to push an amount of fluid corresponding to the SV. A manual bilge pump (figure 25) has been chosen as the first element of the test bench. It will be deprived by the manual lever and thanks to the movement controlled by the actuator, will be able to raise and lower its internal membrane and to push the fluid correspondent to the SV in the ventricular chamber.

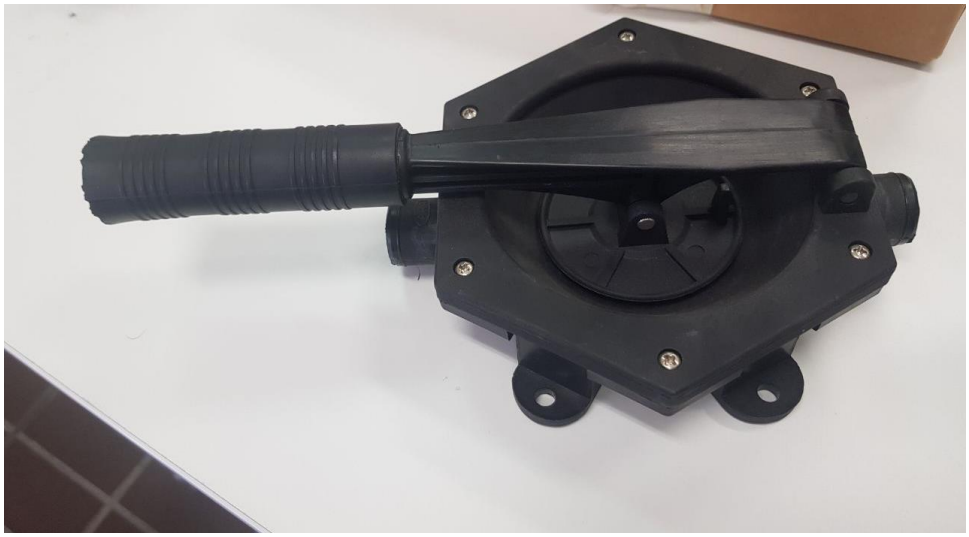


Figure 25. Manual bilge pump.

The stroke of the pump is 20 mm and the diameter is 70 mm. From these parameters, the area and the force have been calculated to find the right actuator.
After finding the instantaneous force and the velocity required for the reproduction of the cardiac cycle, the Linear Actuator from the Linak industry has been selected. In particular, the LA12-IC model has been chosen due to its maximum force of 750 N, to its stroke volume which goes from 19 to 130 mm, and to the position feedback (figure 26). This actuator has an integrated controller and a mechanic potentiometer included. So it respects the required characteristic for which, attached to a pump, will be able to move the necessary quantity of fluid.

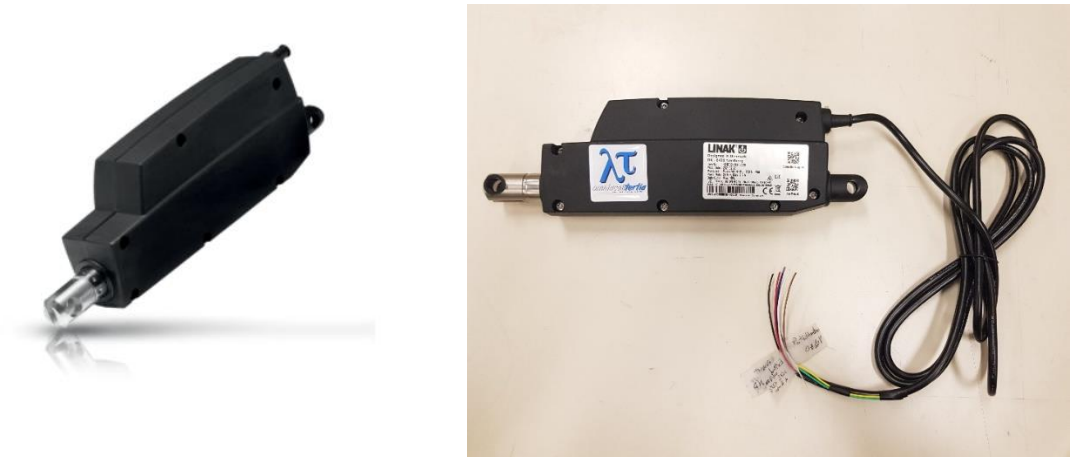


Figure 26. Linear actuator Linak LA12-IC

The actuator-pump complex constitutes the system pump and this coupling recreates an artificial ventricle which well reproduces the pulsatile flow of the heart. The movement takes place according to the law imposed by the computer on the motor, which reproduces the real volumetric variations of blood flow during a complete cardiac cycle, so in systolic and diastolic phases. In particular, when the membrane goes down, it physiologically represents the ventricular ejection period, i.e. the systole, while the retrograde movement is representative of the diastole.
The entire structure is anchored to a Plexiglas panel, which constitutes a wall of the ventricular chamber, through a PLA 3D printed support.

The ventricular chamber is the first tank involved in the circulation. It represents the departure and the arrival chamber of the fluid mass moved by the motor within the closed circuit. Hydraulically speaking, the evolution of fluid mass and the pressures inside this chamber determine the operation of the whole system. One of the six panels composing the ventricular chamber presents a hole for the connection with the pump support and the horizontal superior panel has another hole for the support of the complex left ventricle-aorta. The thickness of the plexiglass panel is about 8 mm and its dimensions are 198x198 mm.
Just above the ventricular chamber, there is the compliance chamber, which contains the aorta and two 3D printed tubes: one that lets flow the blood into the reservoir

from the aorta and one to allow the blood to flow back into the ventricle from the reservoir. The compliance chamber aims to simulate the main features of the human systemic circulation of a healthy subject, such as the elasticity of the larger vessels and resistances applied by peripheral vessels. The larger vessels must be considered in the circuit as the arteries of greater diameter undergo not negligible radial deformations due to ventricular pressure. This effect makes the blood flow to the peripheral vessel almost constant compared to the initial pulsatile motion generated by the heart. The peripheral vascular resistances originate from the very high number of branches that the blood encounters in its motion. The simulated circuit recreates these characteristics using a closed Plexiglas chamber just around the aorta. It contains fluid and pressurized air and these components can damp the pressure wave generated by the motion of the pump, producing a more regular and less impulsive valley wave. The oscillation of the level of fluid in the compliance chamber generates a change in air pressure: the lower the change in air pressure, the higher the initial air pressure. The compliance chamber exploits the compressibility of the air to absorb the pressure wave during the ejection phase and damping the pressure peak and returning the accumulation flow, during the diastole phase, with a more regular trend. The tightness of the plexiglass walls is guaranteed by gluing with a specific bi-component glue suitable for Plexiglass. The panels have a dimension of 150x198 mm, with a thickness of 8 mm. A squared ledge has been printed to guarantee a connection between the ventricular and the compliance chambers.

The fluid, after the narrowing performed by the hydraulic resistance, reaches the last chamber, which is a reservoir. This tank is composed of five panels of plexiglass, glued with special bi-component glue. One of the lateral panels has the inlet and the outlet holes to the tank: the inlet one is connected to the conduct arriving from the compliance chamber; the outlet one instead, is connected to the conduct arriving into the ventricle, effectively closing the fluid cycle. The dimension of the reservoir is such as to dampen the pulsatility of the motion, as the entry of the flow rate doesn’t change the level of fluid. This chamber has the role to send the liquid to the initial

section in the second half of the cycle. In the withdrawal phase of the membrane, flow is taken from the reservoir, activating the mitral valve by creating lower pressure in the ventricle chamber than the static one in the reservoir chamber.

2.5 Extraction of anatomical components

The left ventricle is one of the most important components of the test bench. It is fundamental for the test of the cardiac valve since from it, the fluid that simulates the blood flows through the aortic valve to reach the aortic arc. In this work, a realistic ventricle has been used to mimic as much as possible the physiological characteristics of the organ. A Thoracic Computed Tomography Angiography of an adult woman has been used and only the cardiac region has been selected. *3D slicer* program was used to visualize and modify the DICOM file. In particular, some commands such as "Segment Editor-Grow from seeds", "Hollow" and "Segmentation" have been used to select only the left ventricle and the aorta (figure 27). From the Tomography, only the external walls of the ventricle and aorta have been selected in order to obtain an empty 3D solid, able to contain the blood. The thickness used for the reconstruction of the 3D solid is 3 mm, lower than the real thickness of the ventricle. This choice has been done considering the elastic properties of the material, which changes based on the thickness. A compromise between the physiological parameters and the elasticity of the material has been done in order to allow the ventricle and the aorta to contract and relax through the change of pressure.

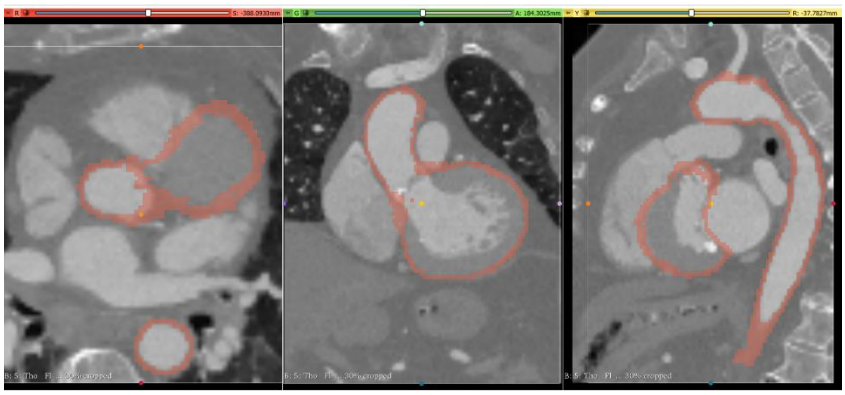


Figure 27. The left ventricle and aorta surfaces selected from the Thoracic Tomography Angiography

After the selection of the organs and of their thickness, all coronaries present on the external surface of the left ventricle and aorta have been deleted to obtain a smooth object (figure 28). This has been an important passage in order to avoid some holes on the surface of the solid during the printing and also to have more homogenous walls during the contraction and relaxation phase. Also, the small arteries starting from the aorta have been removed because, in this first version of the bench, only the aorta is considered as a blood vessel. From each slice of the Tomography, the holes of the arteries have been closed by adding a layer of thickness on the outline of the aorta. In this way, a uniform closed 3D solid has been obtained and the file has been exported as .stl in order to be modified on CAD programs.

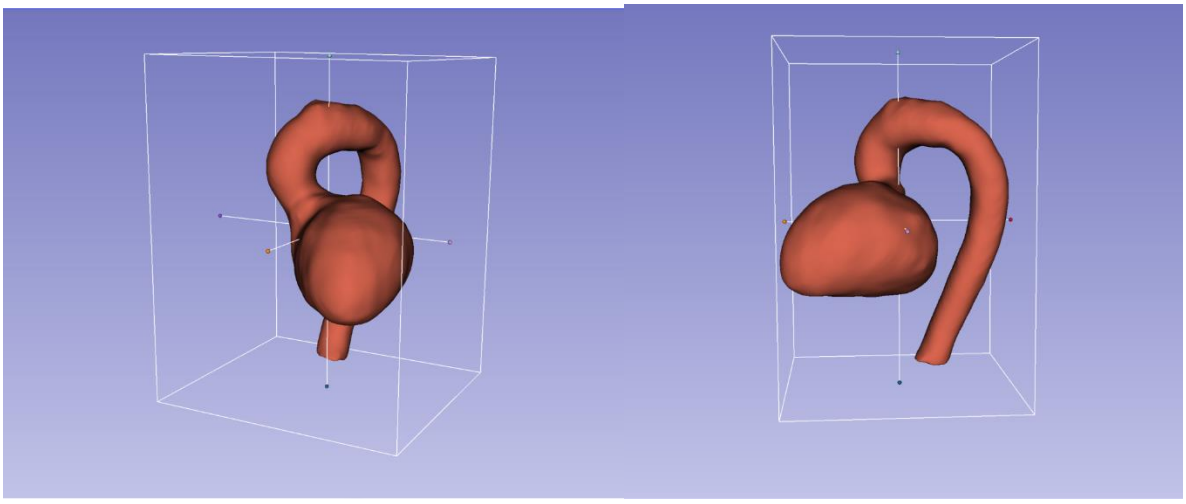


Figure 28. Smoothed surfaces of left ventricle and aorta.

Subsequently, the join of all the meshes composing the object has been performed from *Rhinoceros6* and *AutoCad* (figure 29) so that it can be converted into 3D solid.

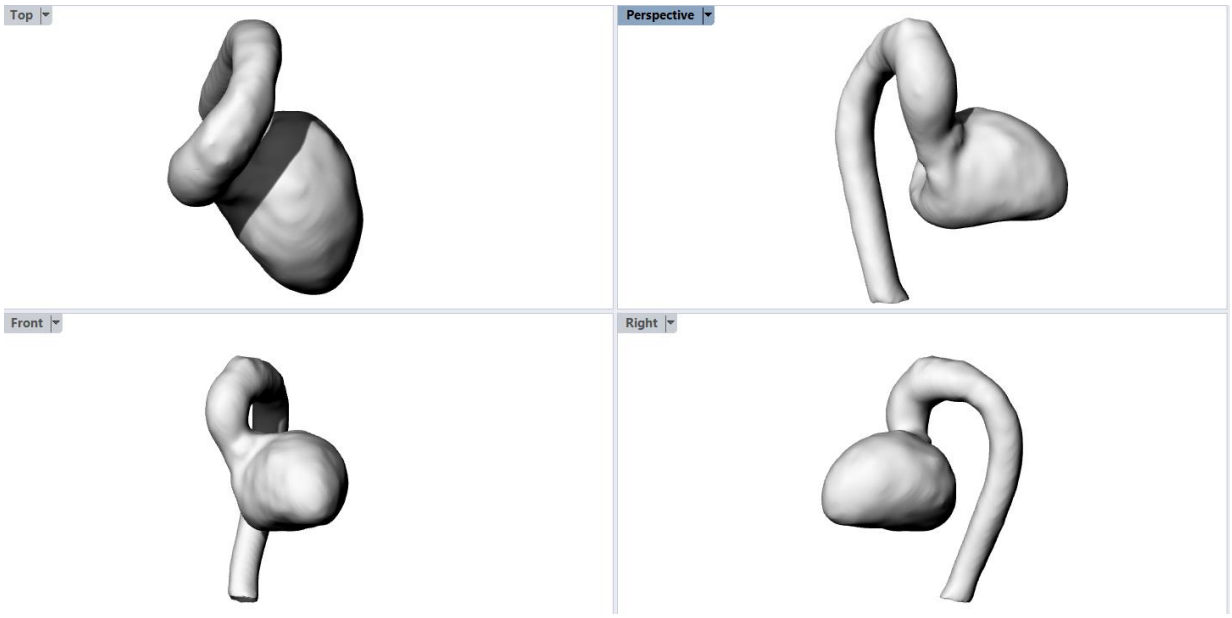


Figure 29. 3D solid of left ventricle and aorta obtained from CAD programs.

Only after these passages, the solid has been modified on *Solid Edge 2022* obtaining adequate housing for the mitral and aortic valves and also a protrusion to ensure the fastening between 3D solid and 3D printed.

2.6 3D printing of anatomical components

By using several commands on *Solid Edge 2022* left ventricle and aorta have been modified on the valves sites. In particular, housing for both mitral and aortic valves is necessary in order to fix them into a precise position and to ensure that they don't move during the changes of pressure when the fluid will be moved through them. Moreover, a protrusion has been revealed to be necessary to fix the solid into the ventricular chamber without touching the Plexiglas panels. For this reason, a protrusion around the external surface of the aortic valve has been done so that the solid can be attached to a support mounted on the upper horizontal panel between the ventricular and the aortic chamber (figure 30).

Figure 30. The protrusion was added between the left ventricle and the aortic arch.

The modification of the internal part of the left ventricle has been a fundamental passage to allow the insertion of the mitral and aortic valves into the appropriate location. Excavations and protrusions have been made through *Solid Edge 2022* so that the mitral valve can correctly be positioned between the ventricle and the pipe from which the fluid will arrive and the aortic valve can be located in the thickening between the ventricle and the initial part of the aortic arc (figure 31).

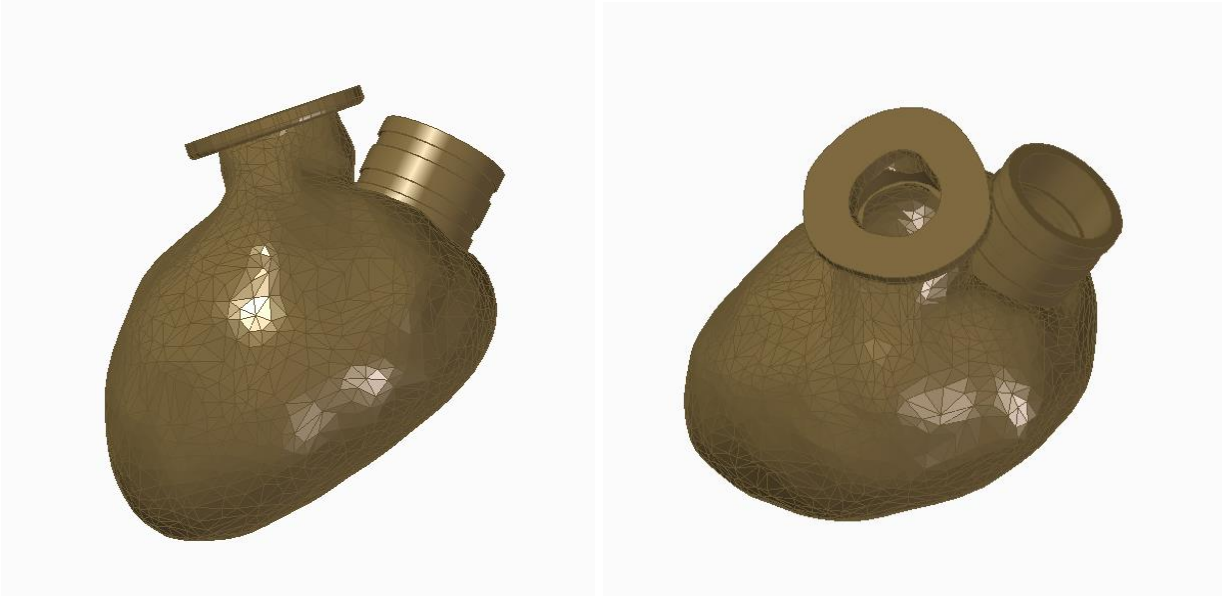
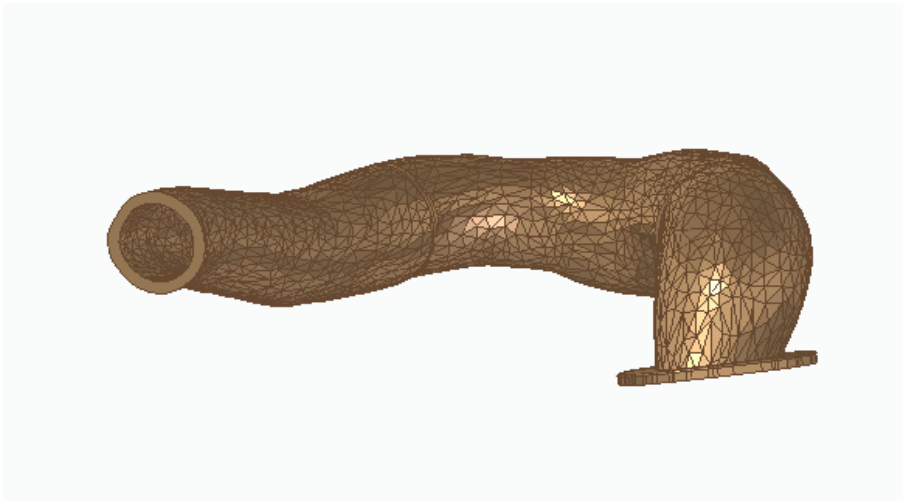
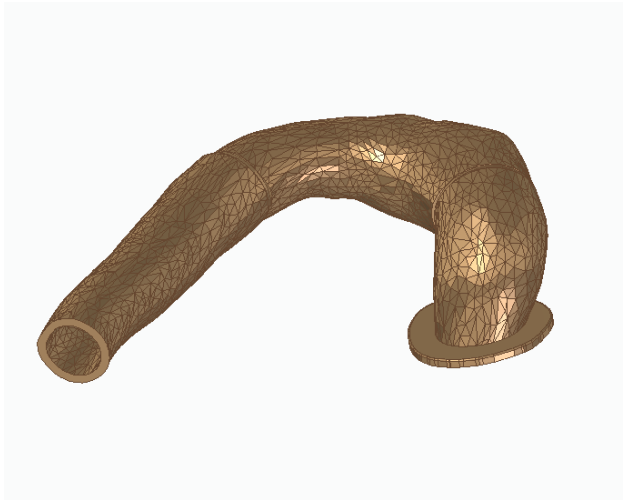


Figure 31. Left ventricle after modifications for the insertion of the valves and the tubes.

Going more in detail about the ventricle, as it is shown in figure 32, the protrusion at the level of the aortic valve has been divided in order to be easily inserted into the hole of the appropriate support and also to allow the insertion of the aortic valve into its site. Through a flange around the aortic valve just above the protrusion, the valve will result fixed and no loss of blood is guaranteed. As regards the mitral valve, instead, its site has been designed through some circular protrusion and excavations inside the tube created to ensure a good connection with the tube that will bring the fluid back into the ventricle. The remaining part of the ventricle remained unchanged to guarantee the real anatomical morphology.

Aorta has been modified on *Solid Edge 2022* to be inserted into the compliance chamber (figure 32). For this reason, its direction has been changed so that it is possible to let flow the fluid directly into the reservoir.





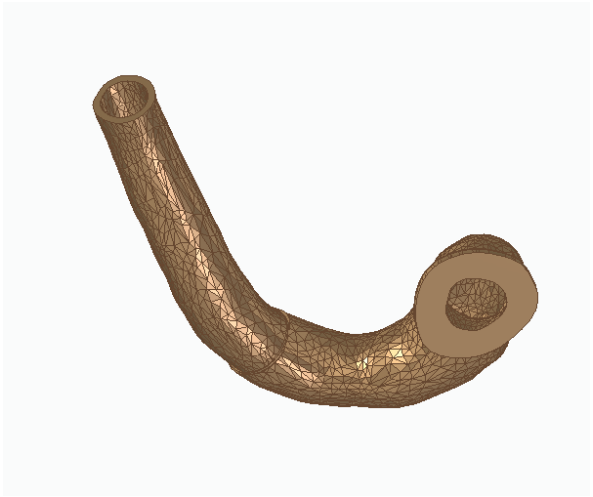


Figure 32. . Aorta after modification on Solid Edge 2022

As for the aortic valve used in this bench, different kinds of models have been used. In particular, an aortic valve was designed on *Solid Edge 2022* with the three cusps that mimic the physiology of the valve, to reproduce the valvular function also (figure 33).

Figure 33. Aortic valve designed on Solid Edge 2022

Furthermore, a bileaflets mechanical valve has been used for the first development of the bench in order to adjust all pressures of the bench before inserting the biological valves and Valve-in-Valve to don't damage them (figure 34).

Figure 34. Aortic valve used in the present test bench

As regards the mitral valve, a mechanical valve has been chosen to be used for all the trials that will be done changing only the aortic valve (figure 35).

Figure 35. Mitral valve used in the present test bench.

The previously mentioned support for the 3D solid has been designed on *Solid Edge 2022* and it is composed of 3 holes: one that follows the outline of the aorta at the level of the created protrusion, so that its half can be inserted, from below, in the upper part of the support; the second hole is composed by a small tube in order to

allow the insertion of a tube above the mitral valve; the third hole has the role to support a cap which allows putting the fluid into the ventricular chamber (figure 36). The support has a circular shape so that it can be easily attached to the upper plexiglass panel of the ventricular chamber and can be removed when heart valves need to be changed. This is possible due to the use of some screws screwed into the six small holes along the edges of the support. The used screws are non-ferromagnetic to guarantee the possibility to perform MRI techniques.

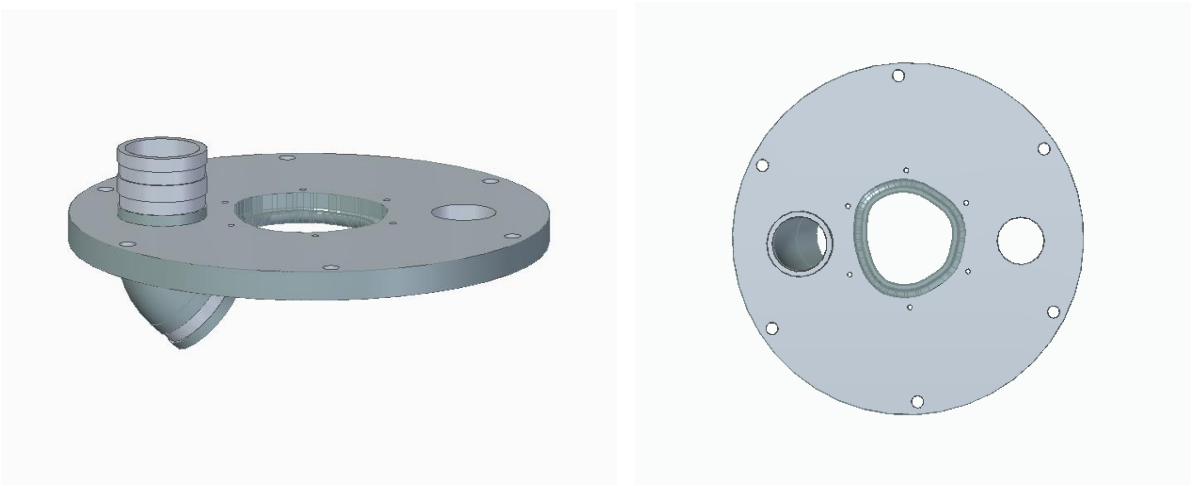


Figure 36.CAD model of the support for left ventricle and aorta.

Moreover, other components have been designed on *Solid Edge 2022* in order to be printed.

A squared ledge has been designed following the dimensions of the ventricular and compliance chamber so that the panels of both the chambers can be inserted into the created excavation to guarantee a watertight (figure 37). It is also useful to lay the compliance chamber directly above the ventricular one.

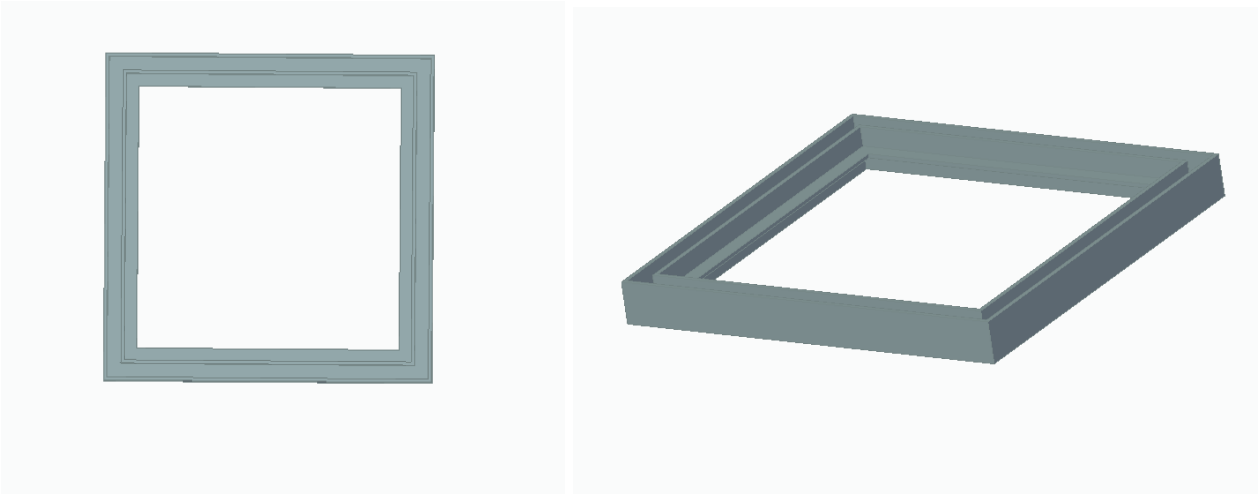


Figure 37. Ledge designed on Solid Edge 2022

Furthermore, support for the pump has been designed in order to allow the connection between the left ventricular chamber and the membrane of the pump (figure 38). In fact, the superior part is adapted as a case for the membrane and the inferior part is suitable to be joint to the Plexiglas panel.

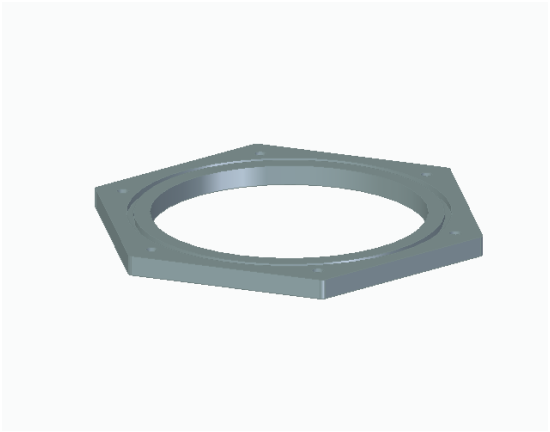


Figure 38. Support for the membrane of the pump, designed on Solid Edge 2022.

Both of them can be observed into the figure 39 during the 3D printing process on the Ender5 Creality 3D printer. The used material has been the PLA and its rigidity has allowed having good supports in the assembly phase.

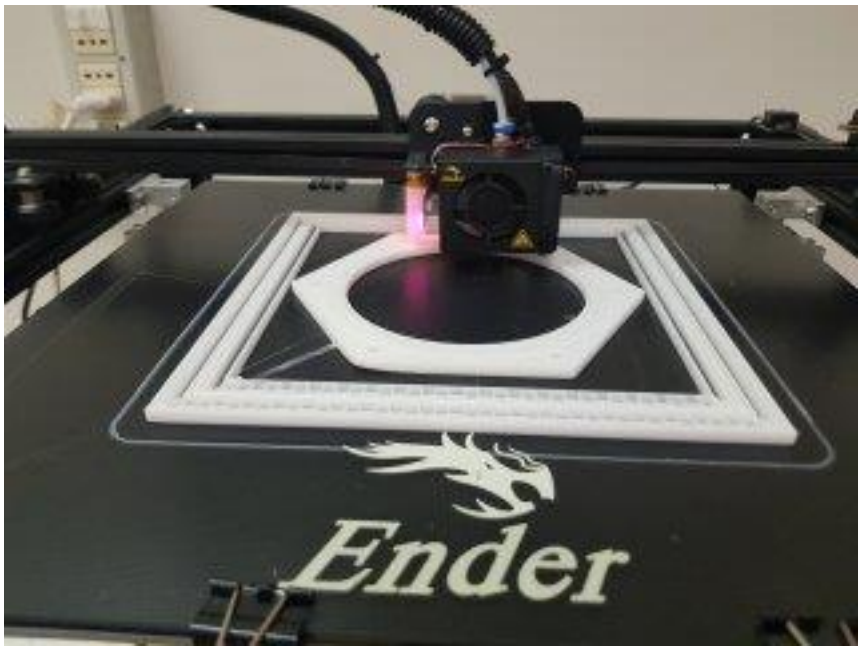


Figure 39. 3D printing of ledge and support for the membrane of the pump.

.

Finally, two curved tubes have been designed in order to let flow the fluid from the reservoir to the ventricle at the level of the small tube created above the mitral valve (figure 40).

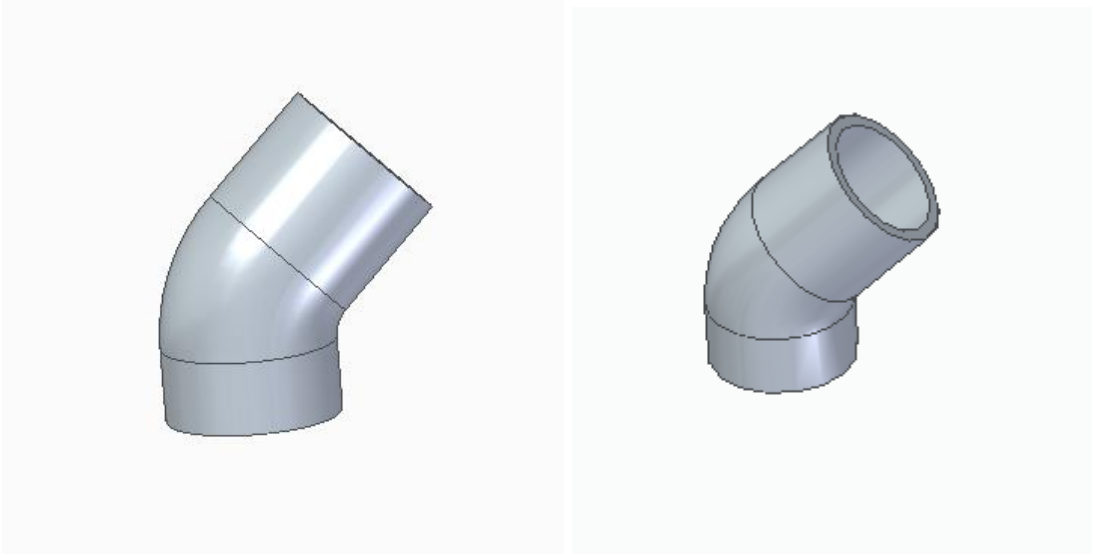


Figure 40. Curved tube designed on Solid Edge 2022.

3. Results

All the previously described passages lead to the development of a test bench for transcatheter aortic valve and Valve-in-Valve. A closed-circuit able to simulate the systemic circulation has been realized starting from the classical procedures found in literature and then adding innovative parts in order to obtain results as close as possible to the physiological ones. The realized bench is composed of all the necessary chambers and components such as hydraulic resistances and compliance, which help to regulate the changes of pressure in the left ventricle and the aortic arc in order to perform studies on the aortic valve. The innovative elements instead are the left ventricle and the aorta which have been realized based on the Thoracic Tomography Angiography of an adult woman. Moreover, the compliance chamber has been mounted directly on the ventricular one so that, thanks to the elastic properties of the aorta, the compliance can directly regulate the value of the afterload, due to the peripheral vascular resistance.

The whole circuit can be appreciated in figure 41.

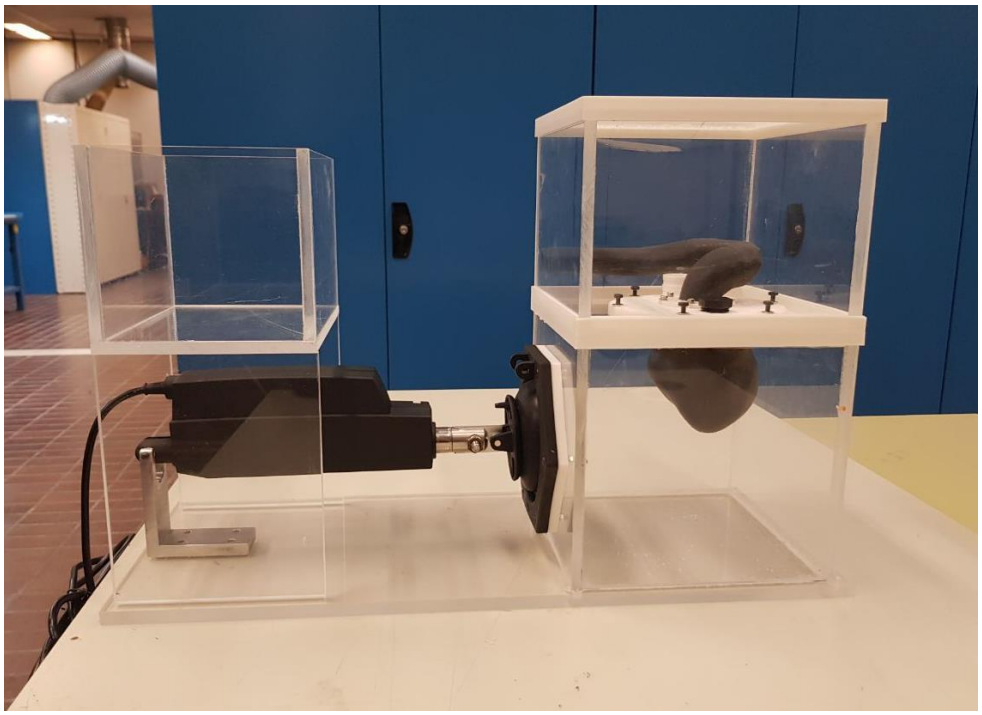


Figure 41. Complete development of the test bench.

As it can be observed, the circuit starts with an actuator able to push and pull the membrane of a pump to move a certain amount of fluid contained into the ventricular chamber, during a cardiac cycle. The considered cardiac cycle duration has been 0,8 seconds, correspondent to 75 bpm, as a real heart rate.

The ventricular chamber has been realized with four plexiglass panels, stuck into a bigger and thicker Plexiglass panel. One of the four walls has been holed in order to allow the pump to push and pull the fluid. In this way, the left ventricle can be compressed and relaxed due to the change of pressure into the ventricular chamber, controlled by the linear actuator attached to the pump.

The left ventricle has been printed with an elastic material of Formlabs, named Flexible for the first assembly tests in order to verify the correct functioning of the bench. Thanks to its elastic characteristic, it can compress to mimic the ejection of the left ventricle, pushing 70 ml of fluid (Figures 42 and 43).

Figure 42. 3D printed Left ventricle with supports due to the Formlab printer.

Figure 43. 3D printed left ventricle from different points of view.

The chosen thickness has been about 3 mm as the first trial in the choice of coupling thickness-elasticity of the material.

Aorta, as well as the left ventricle, has been printed with Flexible, an elastic material of Formlabs (figure 44 and 45). Its elastic characteristics allow the aorta to expand and recoil when the pulsatile flow of the fluid arrives through the aortic valve. One of

its two extremities is used to fix the aortic valve into its specific position and to avoid fluid leaks; the other extremity is connected with a small tube that allows the flow to exit from the compliance chamber and to go to the reservoir.

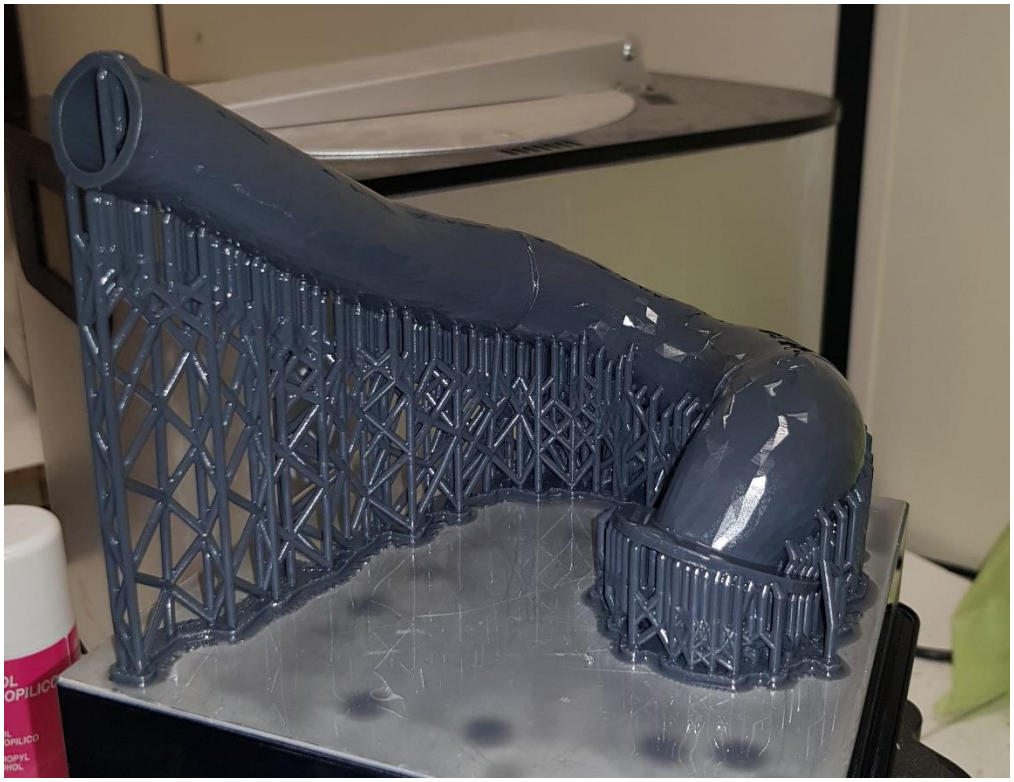


Figure 44. 3D printed aorta with the supports due to the Formlab 3D printer.

Figure 45. 3D printed aorta

The support for the 3D solid has been printed with PLA material and then, a thread has been performed in order to insert a cap which is useful to pour the fluid into the ventricular chamber.

The result of the PLA support connected to the ventricle is shown in figure 46. It has been attached, through some screws, to the horizontal plexiglass panel of the ventricular chamber, which has been previously drilled.

Figure 46. 3D printed left ventricle and support for ventricle and aorta.

The ventricular chamber with the left ventricle inside it, the aorta, and the support which allow maintaining them suspended in order to allow the contraction and the relaxation due to the change of pressure, are shown in figure 47. The compliance chamber has been positioned and fixed above the ventricular chamber to guarantee the watertight and regulate the value of the pressure through the compressed air inside it and the hydraulic resistances located between the compliance chamber and reservoir.

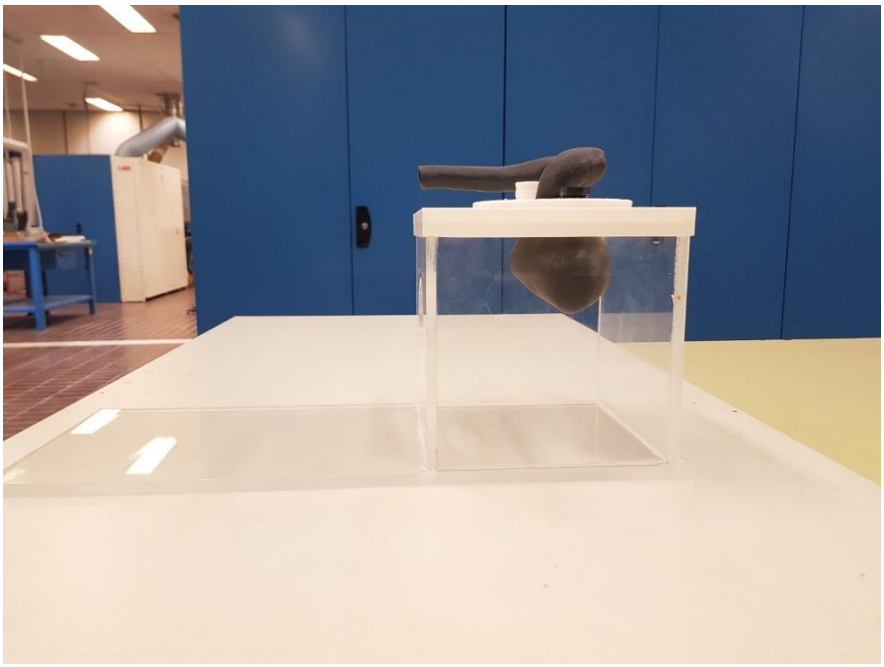


Figure 47. Ventricular chamber and 3D printed left ventricle, aorta, support, and ledge

The last component that has been 3D printed is the biological-like aortic valve (figure 48). Its leaflet can open and close due to the elastic components of the flexible material with which it has been printed and it could be a good solution during the simulation of pathological valves.

Figure 48. 3D printed aortic valve with printing supports (left) and without support (right).

4. Discussion and Conclusion

In this thesis work, a test bench for transcatheter aortic valve and Valve-in-Valve has been developed. Additive manufacturing techniques have been used to realize some bench elements and left ventricle and aorta, which are the main components. Due to the flexibility of the material, these two latter ones can simulate the behavior of the cardiac organ in the systemic circulation activity.

During the development phase, all the requirements and the necessary characteristics to perform measurements techniques have been taken into account. Electromagnetic flowmeters, pressure sensors, and optical measurements instruments could be used in order to obtain all the dynamic information which will help the physiological evaluation of the resulting parameters.

The performing test on the present bench can be considered a tailored-patient test since the morphological and pathological conditions of the patient can be stimulated through the use of Tomography Angiography to reproduce 3D printed anatomical components. In this way it is possible to evaluate which are the operatory risks for each patient, allowing the cardiologists to do practice on the bench and to observe how the hemodynamic changes as the aortic valve position or the diameter of the Valve-in-Valve change.

In order to improve the contraction-relaxation performance of the left ventricle and aorta, more flexible and softer materials can be used, such as Elastic 50A Resin Formlab material. It can be suitable for trials in which the fatigue resistance of the aortic valve is performed by increasing the heart rate parameter, but also simulating pathological conditions such as hypertension, in which pressure in the ventricle is very high.

In conclusion, it is expected that the present test bench will provide reliable physiological parameters with the objective to perform several unfailing tests on various types of aortic valves.

Attachment

The left ventricle volume, pressure, and aortic pressure have been obtained from the following Matlab code:

```
%load curves
I_vol=imread('volume_ventricolo.jpg');
I_pres=imread('pressione_ventricolo.jpg');
I_pres_ar=imread('pressione_arteriosa.jpg');

I_vol=I_vol(:,:,3);
I_pres=I_pres(:,:,3);
I_pres_ar=I_pres_ar(:,:,3);

mm=min(size(I_pres,1),size(I_vol,1));
mn=min(size(I_pres,2),size(I_vol,2));

I_vol=I_vol(:,1:mn);
I_pres=I_pres(1:mm,:);

%left ventricle volume curve
for ii=1:mn
    [m ind]=min(I_vol(:,ii));
    aa=I_vol((ind-1):(ind+1),ii);
    vv(ii)=ind+double((aa(1)-aa(3)))/double((2*(aa(1)-
2*aa(2)+aa(3))));

    v(ii)=ind;
    dd(ii)=m;
end

fine=max(find(dd>10));
v=v(1,1:fine);
v=-v;

vv=vv(1,1:fine);
vv=-vv;


%left ventricle pressure curve
for ii=1:1:mn
    [m ind]=min(I_pres(:,ii));

    bb=I_vol((ind-1):(ind+1),ii);
    pp(ii)=ind+double((bb(1)-bb(3)))/double((2*(bb(1)-
2*bb(2)+bb(3))));
end
```

```
pp=pp(1,1:fine);
pp=-pp;

%arterial pressure curve
for ii=1:1:mn
    [m ind]=min(I_pres_ar(:,ii));
    cc=I_vol((ind-1):(ind+1),ii);

    ppp(ii)=ind+double((cc(1)-cc(3)))/double((2*(cc(1)-
2*cc(2)+cc(3))));
end

ppp=ppp(1,1:fine);
ppp=-ppp;


bpm=75;
T=60/bpm;
f=1/T;
F=f*5;
dt=T/mm;

%coordinates
%ventricle volume
Y_vol=(   vv-min(vv))  /(   max(vv)-min(vv)     );

vol_min=50;
vol_max=120;
Y_vol=Y_vol*(vol_max-vol_min)+vol_min;

t_min=0;
t_max=T;

X=[1:fine];
X=(   X-min(X))  /(   max(X)-min(X)     );
X=X*(t_max-t_min)+t_min;
Y_vol=movmean(Y_vol,10);

figure, plot(X,Y_vol)
xlim([0,0.80]);
ylim([45,130]);
xlabel('time(s)');
ylabel('volume(ml)');

%ventricle pressure
Y_pres=(   pp-min(pp))  /(   max(pp)-min(pp)     );

pres_min=5;
pres_max=120;
```

```
Y_pres=Y_pres*(pres_max-pres_min)+pres_min;
Y_pres=movmean(Y_pres,10);

figure, plot(X,Y_pres);
xlim([0,0.80]);
ylim([0,130]);
xlabel('time(s)');
ylabel('pressure(mmHg)');

%arterial pressure
Y_pres_ar=(   ppp-min(ppp))  /(   max(ppp)-min(ppp)     );

pres_min_ar=80;
pres_max_ar=120;

Y_pres_ar=Y_pres_ar*(pres_max_ar-pres_min_ar)+pres_min_ar;
Y_pres_ar=movmean(Y_pres_ar, 10);

figure, plot(X,Y_pres_ar)
xlim([0,0.80]);
ylim([70,130]);
xlabel('time(s)');
ylabel('pressure(mmHg)');
```

The part of code used to calculate SV and CO is:

```
%% stroke volume
max_vol=max(Y_vol);
min_vol=min(Y_vol);
dV=max_vol-min_vol; %ml/s

%cardiac output
Cardiac_output=-Y_vol/T; %ml/s
Cardiac_output=Cardiac_output+150;

figure, plot(X, Cardiac_output)
xlabel('time(s)')
ylabel('ml/s')
```

Matlab code used for the calculation of force and velocity of the actuator.

```
diameter=70*10^-3; %m
area=(pi*diameter^2)/4; %m^2;
```

```
%force
Force=Y_pres*area; %N
Force_max=max(Force);

%velocity
Velocity=CO/area; %m/s
Vel_max=max(Velocity); %m/s
figure, plot(X,Velocity);
xlabel('time(s)');
ylabel('velocity(m/s)');
```

5. Bibliography

[1] IQWiG (Institute for Quality and Efficiency in Health care), “informedhealth.org.” Cologne, Germany, 2006.

[2] R. B. Hinton and K. E. Yutzey, “Heart valve structure and function in development and disease,” *Annual Review of Physiology*, vol. 73, pp. 29–46, 2011, doi: 10.1146/annurev-physiol-012110-142145.

[3] J. D. Humphreyl and A. D. Mcculloch, “The Cardiovascular System-Anatomy, Physiology and Cell Biology.”

[4] Heba Soffar, “Cardiac cycle importance, phases, diastole & systole, Aortic pulse curve & jugular venous,” Apr. 30, 2021.

[5] D. Sadava, G. Heller, G. Orians, W. Purves, D. Hillis, and M. Pignocchino, *Biologia Blu*. 2021.

[6] E. Niemann and S. Blatt, “Winkessel Model Analysis: Blood Pressure in Response to Blood Flow,” 2018.

[7] F. Sacco *et al.*, “Left ventricular trabeculations to decrease the wall shear stress and increase the intra-ventricular pressure drop in CFD simulations,” *Frontiers in Physiology*, vol. 9, Apr. 2018, DOI: 10.3389/fphys.2018.00458.

[8] K. Hayashida *et al.*, “True Percutaneous Approach for Transfemoral Aortic Valve Implantation Using the Prostar XL Device Impact of Learning Curve on Vascular Complications,” 2012.

[9] A. S. Petronio *et al.*, “Safety and efficacy of the subclavian approach for transcatheter aortic valve implantation with the CoreValve revalving system,” *Circulation: Cardiovascular Interventions*, vol. 3, no. 4, pp. 359–366, Aug. 2010, doi: 10.1161/CIRCINTERVENTIONS.109.930453.

[10] “Impianto percutaneo transcatetere della protesi valvolare aortica (TAVI),” *Humanitas Gavazzeni*.

[11] C. D. Miller, “Procedura ‘valve-in-valve’ per la correzione transcatetere delle bioprotesi aortiche degenerate A cura di Antonella Potenza,” 2017.

[12] J. T. Saxon, K. B. Allen, D. J. Cohen, and A. K. Chhatriwalla, “Bioprosthetic valve fracture during valve-in-valve TAVR: Bench to bedside,” *Interventional Cardiology Review*, vol. 13, no. 1, pp. 20–26, 2018, DOI: 10.15420/icr.2017:29:1.

[13] M. Simonato *et al.*, “In vitro evaluation of implantation depth in valve-in-valve using different transcatheter heart valves,” *EuroIntervention*, vol. 12, no. 7, pp. 909–917, Sep. 2016, DOI: 10.4244/EIJV12I7A149.

[14] E. Knott, H. Reul, M. Knoch, U. Steinseifer, and G. Rau, “In vitro comparison of aortic heart valve prostheses”.

[15] R. de Paulis, C. Schmitz, R. Scaffa, P. Nardi, L. Chiariello, and H. Reul, “In vitro evaluation of aortic valve prosthesis in a novel valved conduit with pseudosinuses of Valsalva,” *Journal of Thoracic and Cardiovascular Surgery*, vol. 130, no. 4, pp. 1016–1021, Oct. 2005, DOI: 10.1016/j.jtcvs.2005.04.028.

[16] G. Querzoli, S. Fortini, S. Espa, M. Costantini, and F. Sorgini, “Fluid dynamics of aortic root dilation in Marfan syndrome,” *Journal of Biomechanics*, vol. 47, no. 12, pp. 3120–3128, Sep. 2014, DOI: 10.1016/j.jbiomech.2014.06.025.

[17] G. Querzoli, S. Fortini, S. Espa, and S. Melchionna, “A laboratory model of the aortic root flow including the coronary arteries,” *Experiments in Fluids*, vol. 57, no. 8, Aug. 2016, DOI: 10.1007/s00348-016-2221-x.

[18] O. Bazan and J. P. Ortiz, “Experimental validation of a cardiac simulator for in vitro evaluation of prosthetic heart valves,” *Brazilian Journal of Cardiovascular Surgery*, vol. 31, no. 2, pp. 151–157, Mar. 2016, DOI: 10.5935/1678-9741.20160041.

[19] W. Feng, X. Yang, Y. Liu, and Y. Fan, “An In Vitro Feasibility Study of the Influence of Configurations and Leaflet Thickness on the Hydrodynamics of Deformed Transcatheter Aortic Valve,” *Artificial Organs*, vol. 41, no. 8, pp. 735–743, Aug. 2017, DOI: 10.1111/aor.12833.

[20] W. Y. I. Tseng, M. Y. M. Su, and Y. H. E. Tseng, “Introduction to cardiovascular magnetic resonance: Technical principles and clinical applications,” *Acta Cardiologica Sinica*, vol. 32, no. 2, pp. 129–144, Mar. 2016, DOI: 10.6515/ACS20150616A.