UNIVERSITY OF STRATHCLYDE –
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Master of Science Dissertation

Early prototyping and testing of a model of an expandable heart valve apparatus for paediatric deployment.

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This thesis is the result of the author's original research. It has been composed by the author and has not been previously submitted for examination which has led to the award of a degree.

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Abstract

Valvular heart disease is any abnormal condition which involves one or more of the heart valves – the aortic and mitral valves on the left and the pulmonary and tricuspid valves on the right. Valves diseases in infants are congenital and their effect is to burden the heart with an increased work to maintain the stroke volume what might result in heart muscle dysfunction and potential congestive heart failure. There are two main possibilities of the treatment of those abnormalities – heart valve repair and heart valve replacement, both of which might be very complicated. If a child needs a replacement of the heart valve, there are only a limited number of options available, all of which have one limitation in common: they have a fixed diameter and cannot grow with an infant. Unlike traditional prosthetic heart valves, the expandable valves can be enlarged while the patient grows. Such solution potentially allows avoiding the repeated valve replacement procedures that would be required when traditional valve is implanted.

The aim of this study was to design nine different pulmonary valve models based on the concept of expandable heart valve apparatus for paediatric application, and to test their performance through Computational Fluid Dynamic simulation using Finite Volume Method. The obtained results including pressure distribution, velocity and wall shear stress were analysed, and the optimal heart valve model was recommended.

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1. Heart Valve Diseases

Human heart consists of two pairs of one-way valves that prevent the backflow of blood as the chambers contract: the atrioventricular valves and the semilunar valves (figure 1). The atrioventricular valves are situated between the atria and the ventricles. They include the right atrioventricular valve also known as tricuspid valve and the left atrioventricular valve also known as mitral or bicuspid valve. The semilunar valves which guard the outflow from two ventricles include the aortic and pulmonary valves. They are called semilunar valves because of the half-moon shape of their leaflets (Martini et al., 2014).

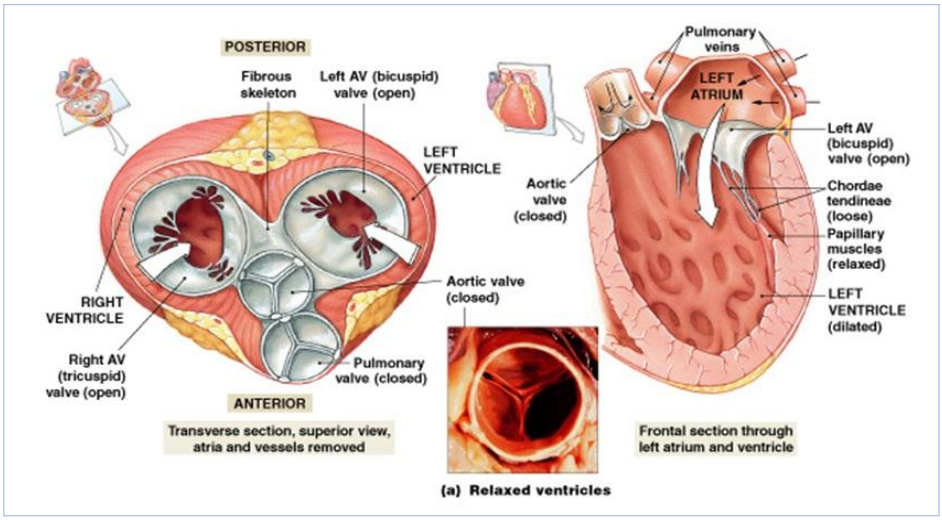


Figure 1. Valves of the heart presented during relaxation of the ventricles (Martini et al., 2014).

All of the heart valves enable the blood flow in one direction. Oxygen-depleted blood returns from the body via the venae cava to the right atrium and through the tricuspid valve to the right ventricle. It then flows through the pulmonary valve to the pulmonary artery, and to the lungs. Oxygenated blood from the lungs returns via pulmonary veins to the left atrium and through the mitral valve to the left ventricle. It then goes through the aortic valve to the aorta, and finally to the rest of the body. The flow of the blood is achieved by the pumping action of the heart. During ventricular ejection, aortic and pulmonary or pulmonic valves remain open and mitral and tricuspid valves remain closed, and during ventricular filling, aortic and pulmonary valves remain closed and mitral and tricuspid valves remain open. Dis-

turbance in the normal ventricular ejection and/or filling in most cases has its origin in valvular disease (Thubrikar, 1990).

Valvular disease or heart valve disease generally is defined as a disorder involving one or more of the valves of the heart which result in improper work of the valves of the human muscular pump, and therefore in disturbed blood flow. There are several ways by which the heart valve can become diseased however they all present themselves as being stenotic, incompetent, or both (Thubrikar, 1990). A stenotic valve is one which offers significant obstruction to the forward flow of the blood (figure 2). Valvular stenosis occurs due to stiff or fused leaflets. The narrowed opening makes the heart work harder to pump blood through it. The severity of the obstruction is evaluated by measuring the pressure drop across the valve and by determining the orifice area. An incompetent valve also called regurgitant, insufficient or leaky valve is a valve disorder which allows blood to move backward across the valve (figure 3). Incompetence occurs when a valve does not close tightly. As the leak worsens, the heart starts working harder to make up for the leaky valve, and less blood may flow to the rest of the body. Valvular stenosis and incompetence are conditions which frequently co-exist (Thubrikar, 1990).

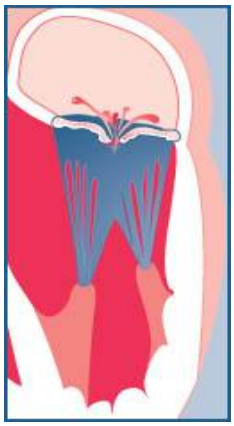


Figure 2. Stenotic valve (left) (Cleveland Clinic, 2010).

Figure 3. Incompetent valve (right) (Cleveland Clinic, 2010).

Valvular heart diseases in infants are congenital meaning that any abnormality of the valve develops before birth and is present at birth, and later in adult life if not treated. It might be associated with improper valve size, malformed leaflets, or an

irregularity in the way the leaflets are attached. This most often affects the aortic or pulmonary valve (Web MD, 2014). Heart valve disease might be also acquired later in life caused by such conditions as coronary artery disease, cardiomyopathy hypertension or heart valve infection. Some patients with heart valve defects or disease do not demonstrate any symptoms. Sometimes the condition mostly stays the same throughout their lives and does not cause any major problems. However for most patients the condition slowly worsens until symptoms develop. If heart valve disease is not treated, the advanced condition might cause heart failure, stroke, blood clots, or sudden death due to sudden cardiac arrest (SCA). Currently, no medicines can cure heart valve disease. However, changes in the lifestyle and medicines can be prescribed to relieve many of the symptoms and problems linked to heart valve disease as well as to lower the risk of the life-threatening conditions such as SCA (National Hurt, Lung, and Blood Institute, 2011)

Some types of congenital heart valve disease can be si severe that the valve must be repaired or replaced during infancy, childhood, or even before birth. Other types may not cause problems until the patient is middle-aged or older, if there is a need at all (What Is Heart Valve Disease?, 2011). The goal of intervention in case of valvular pathology in young patients is valvular repair as the restoration of valvular anatomy and physiology using native tissue allows for growth and a potentially better long-term outcome (Henaine et al., 2012). However, when reconstruction fails or is not feasible, the replacement of the affected valve becomes an only treatment option.

In this paper the main focuses are on the congenital heart valve diseases in infants and children, and the challenges they pose on the paediatric surgeons.

1.1 Repair as a treatment option

Heart valve repair is the preferable treatment option in infants and children as it eliminates problems related to the replacement of the affected valve with prosthe-

sis. It is usually done to treat the congenital defects, and it might include such procedures as (Texas Heart Institute, 2013) :

- *Commisurotomy* – a procedure used for narrowed valves when the leaflets are thickened and stuck together. The objective is to open the valve by cutting the points where the leaflets meet.
- *Valvuloplasty* – performed to open a stenotic heart valve. In valvuloplasty, a very small, narrow, hollow tube called catheter is advanced from a groin artery through the aorta into the heart. Once the catheter is placed in the valve to be opened, a large balloon at the tip of the catheter is inflated until the leaflets of the valve are opened. Once the valve has been opened, the balloon is deflated and the catheter is removed.
- *Reshaping* – introduced when a valve has lost its shape and cannot close completely. During the procedure, a surgeon may cut out a piece of a leaflet so the valve can close properly again.
- *Decalcification* – during this procedure calcium deposits are removed from the leaflets of the valve so that they are able to function normally - the leaflets are able to close properly.
- *Repair of structural support* – replaces or shortens the cords –chordae tendinae and the papillary muscles which provide the support to the mitral valve. When the cords are restored to a proper length, the valve can close properly.
- *Patching* – this procedure is performed if one of the valve leaflets has a hole or tear. The objective is to repair the leaflet defect with a tissue patch.

The procedure used to repair patient's heart valve depends largely on which valve is damaged. Generally, tricuspid and mitral valve are the most frequently repaired heart valves, with a large percent of patients having a successful repair procedure. Aortic and pulmonary heart valves repairs are less readily performed due to a greater risk of complications and nature of the defects. In the case when the repair of the valve fails due to the severe damage of the valve or repair or intervention

failure, and when a person is classified as a high risk patient, the preferable method of treatment is replacement of the native valve with a biological or artificial prosthesis (Medtronic, 2012).

1.2 Replacement of the native heart valve in children

Although in many cases the reconstruction of the diseased / deformed heart valve remains the goal of intervention, valve replacements have become a more popular choice due to the development of materials used and the new approaches of the delivering of the prosthesis. The controversial factor is still which valve is most suitable for which position. The decision is hard to make as both biological and mechanical prostheses demonstrate several advantages and also some disadvantages that might have a great influence on the overall condition of the patient. Choosing the appropriate heart valve prosthesis can be therefore a challenge, and should be based on the patient's individual requirements in order to provide an optimal treatment.

Among congenital cardiac defects, aortic valve disease is one of the most common and it has been assumed that it occurs in 5% of all children with heart disease (Henaine et al., 2012). The second most common valve replaced in the congenital defect population is the pulmonary valve which brings controversy regarding the optimal timing for its replacement, especially in children (Henaine et al., 2012). A review on currently available prostheses in valve replacement in children has been presented below.

1.2.1 Biological prosthesis

Biological valve prostheses also called bioprosthetic valves are designed to mimic the behaviour of natural valves, so that closure and opening of the valve leaflets are obtained by the spontaneous coaption and parting of biological membranes, driven by the blood flow and pressure. Their objective is to replicate patient's native valve, and they are characterised by excellent haemodynamic and thrombogenic perfor-

mances, providing the freedom of anticoagulation therapy (Mohamammadi, 2011). The biological prostheses include autografts, allografts (homografts) and xenografts (heterografts).

a) Autograft and allograft valves: Ross procedure

Ross procedure also known as pulmonary autograft (PA) has been named after Donald Ross – cardiac surgeon who proposed this technique for the first time in 1962. During the operation a diseased aortic valve is replaced with a pulmonary autograft (patient's own pulmonic valve), and in order to replace the pulmonary valve, a pulmonary allograft (valve from human donor) is used. Henaine et al. (2012) pointed out that a pulmonary autograft is characterised by excellent haemodynamic performance, superior longevity, freedom from thromboembolism without the need for anticoagulation and haemolysis, and decreased susceptibility to endocarditis. Another and perhaps the most important advantage of the Ross procedure with regard to children is its potential to grow. Furthermore, it is a versatile operation which might be applied to patients with various left ventricular outflow tract and aortic valve pathologies. Nevertheless, the procedure is also not free from several disadvantages that can limit its application in the congenital disease population. PA is a technically demanding procedure and frequently requires reoperation due to bleeding and postoperative conduction abnormality. Henaine et al (2012) indicated that autograft insufficiency is one of the leading causes of the reoperation with the Ross procedure and pointed factors which increase the risk of failure such as preoperative diagnosis of aortic incompetency, presence of dilated aortic annulus, bicuspid aortic valve, rheumatic heart disease, technical imprecision, the type of insertion and inherent disease of the pulmonary valve. Although the Ross technique have been shown to be safe with the operative mortality being under 2.5% in children, the mortality risk in infants less than 1 year old is much higher and approaches up to 20%. The risk factors in this group of patients included concomitant arch surgery and post-operative ECMO. Alsoufi et al (2013) indicated that despite excel-

lent survival and superior haemodynamics following PA, the recommendations for this procedure has been declining, particularly in older children who can be offered other aortic valve replacement options. The reason for the declining tendency is the concerns about the development of neoartic root dilatation, with or without autograft regurgitation.

Finally, the main disadvantage of this technique is the necessity of implanting two heart valves in order to treat a single valve defect. It means there is a need to replace the native pulmonary valve with a valve from human cadavers. Although homografts come in different ranges, and are associated with excellent haemodynamic profiles, their availability, particularly in the smallest ranges for very young patients, varies due to the limited donor pool.

b) Xenograft valves

Xenograft valves obtained from a donor of different species are typically manufactured from porcine aortic valves or bovine pericardium tissue. Cross species implantation of animal tissues normally would cause immune rejection and rapid tissue degeneration. For this reason, bovine or porcine tissues are treated with glutaraldehyde, a water-soluble cross-linker, which almost completely reduces tissue antigenicity. In addition, glutaraldehyde devitalises tissues and kills all resident cells, prevents degradation by host enzymes, and sterilises the tissue for implantation. Most heterografts are mounted on stents attached to a sewing ring, but more recently stentless valves which are sewn in free hand have become available and more popular. Stentless valves have been found to possess greater effective orifice area compared with stented valves, but on the other hand they are technically more challenging to implant (Mohamammadi, 2011). Xenografts are implanted to replicate the patient's native valve, and they have been found to provide excellent haemodynamic and thrombogenic performances, eliminating the need for anticoagulant therapy. Furthermore, they are readily accessible and come in different ranges however they are unavailable in sizes smaller than 19 mm, making them un-

suitable for infants. Asfoulti et al (2013) pointed out that their use in paediatrics is also limited by decreased valve longevity and frequent need for reoperation due to lack of growth potential with the development of patient-prosthesis mismatch (PPM) and also structural valve degeneration (SVD) which is more rapidly observed in children than adults.

Figure 4. Hancock II Tissue valve obtained from porcine heart (left) (Medtronic, 2010).

Figure 5. Mitroflow heart valve with leaflets from bovine pericardium (right) (Sorin Group, 2014) .

1.2.2 Mechanical prosthesis

The second type of the heart valve prostheses are mechanical heart valve prosthesis also known as artificial valves. As the name indicates they are entirely made of synthetic materials such as titanium, cobalt, LTI carbon, Derlin, Telfon, Dacron etc., and are characterised by one or more stiff moving components that alternately occlude the orifice of a fixed frame. Generally, they possess excellent mechanical properties, allow good consistency of production, and unlike biological prosthesis they are characterised by greater durability. The main components of almost all types of the mechanical valves are a hinge, stent, leaflet and a sewing ring. The development of the mechanical valves for over the last 50 years resulted in such valves as the ball and cage, the disc and cage, the tilting disc, the monoleaflet and the bileaflet heart valves. However, caged valves are no longer implanted and they have been re-

placed by valves with improved haemodynamic profile (Mohamammadi, 2011).

a) Tilting disc valves

Tilting disc valves also known as monoleaflet valves have been introduced to replace the caged-disc valves as the latter ones occurred to be slow in dynamic response to the pulsatile flow of the natural haemodynamic characteristics of the body, and also because their natural haemodynamic properties were weak. Therefore, instead of ball, a caged disc was used to play a role of the leaflet. The earliest examples of the tilting disc valves were flap valves which had a ring with a straight segment along which a disc was hinged. The first disc concept designs were introduced between 1965 and 1967, and involved Cross–Jones, Kay–Shiley and Beall caged disc valves which were used exclusively in mitral and aortic positions. Because of the problems thevalves caused such as obstruction and dynamic back flow, they were withdrawn shortly. Next design was introduced in 1967 which involved a free-floating disc that in the open position tilts to an angle depending on the design of the disc-retaining struts. Finally, an alternative concept called Medtronic-Hall prosthesis was proposed in 1977 (Mohamammadi, 2011).

Tilting disc valves can open at an angle of 60° and at a rate of 70 beats per minute. The angular opening of this valve reduces damage to blood cells. Although they have superior haemodynamic characteristics over the caged ball valves, some models still tend to fatigue and fracture over the long period of time (Mechanical Heart Valve, 2008).

b) Bileaflet valves

Bileaflet valves as the name implies are made of two semilunar discs attached to a rigid valve ring by small hinges. They have been designed to address some of the complications encountered while using tilting disc valves. The opening angle of the

leaflets relative to the annulus plane ranges from 75° to 90°, and the open valve consists of 3 orifices: a small, slit-like central orifice between the 2 open leaflets and two larger semi-circular orifices laterally (Pibarot PhD and Dumensil, 2009). Bileaflet valves are the most protected as the leaflets hardly stick out from the valve ring, even during maximum opening. The large effective orifice area of the bileaflet valves contributes to creating a flat, nearly normal flow profile with far less obstruction and blood flow abnormalities, as compared with earlier generations of replacement valves. Similarly to other mechanical valves, the bileaflet valves are not free from thromboembolism therefore the lifelong anticoagulation therapy is a must. The first bileaflet heart valve prosthesis was introduced by St. Jude Medical Inc. in 1978. This concept includes two semilunar pyrolytic carbon leaflets, which in the opening position are intended to provide disturbance free flow (Mohamammadi, 2011).

Bileaflet prosthesis has been found in general to provide a uniform flow profile and lower level of structural problems. Nevertheless, the bileaflet concept also presented some complications including thrombus formation on hinges, valve failure and leaflet escapement. In addition, the major problem identified was cavitation. It has been found that cavitation at the leaflet surface causes bubble formation and collapse which eventually leads to a failure of the valve (Mohamammadi, 2011).

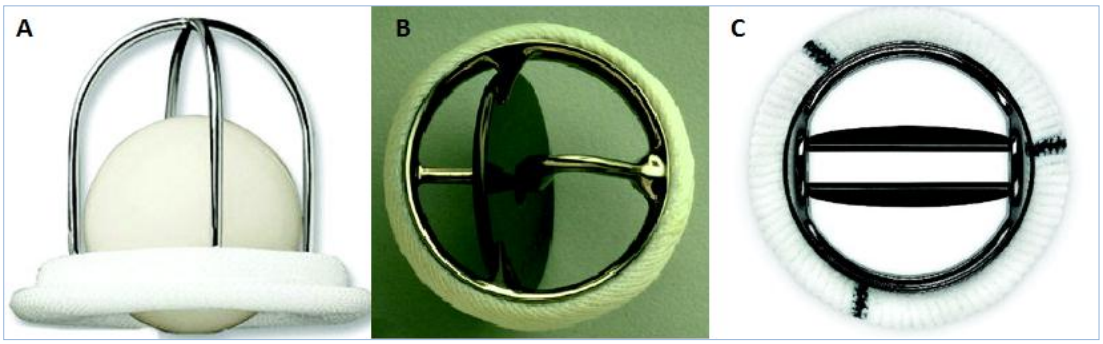


Figure 6. A: Caged-ball heart valve prosthesis designed by Starr Edwards. B: Monoleaflet (tilting disc) heart valve from Medtronic Hall. C: Bileaflet mechanical heart valve introduced by St. Jude (Pibarot & Dumensil, 2009).

1.3 Limitations of the commercially available heart valve prosthesis

Since the first heart valve replacement therapy in 1960s, the mechanical valve prosthesis has transformed from the ball caged valves through the tilting disc prosthesis

to more advanced bileaflet pyrolytic carbon valves. Bioprostheses have also improved from previously unstable formalin-fixed tissue valves to superior prototypes: glutaraldehyde-treated bovine pericardial or porcine aortic valves (Ghanbari, 2009). Although both mechanical and biological prostheses have been used readily within this time, and some improvements have been introduced, no significant clinical outcome has been observed. The main complications related with both types of prosthesis such as thrombogenicity and durability have remained problematic in long-term application. These limitations of the mechanical and biological heart valve prostheses stimulated a number of researchers to explore other solutions which would join the advantages of both valves - provide better haemodynamics, and thus increase durability as well the resistance to thromboembolism. The possible alternative was found to be soft synthetic polymers which have been widely investigated. Although the research and development of polymeric valves has been slow due to initial complications, advances in the material sciences have resulted in superior polymers which in turn drew the attention of the researchers towards polymeric heart valves.

1.3.1 Polymeric heart valves

Polymeric heart valves are another type of mechanical valves as they are made of flexible synthetic materials - polymers. However, the main difference between polymeric and traditional artificial valves is the geometry which in the case of heart valves made of polymers is similar to the natural one, which was a response to the rigid leaflets of the classical mechanical prostheses (Mohamammadi, 2011). The ability of polymeric materials to maintain or mimic natural haemodynamics is based on the fact that they have a flexible structure which simulates the stiffness exhibited by the natural heart valve tissue and allows them to contract and expand freely in conformity to the aortic root movement during cardiac cycle to allow natural blood flow. Another advantage the polymeric valve prostheses have over the other mechanical heart valves (MHVs) is that they have been found to be biocompatible, e.g. they are characterised by improved haemocompatibility (Ghanbari, 2009).

While designing a polymeric heart valve, the crucial element is the material choice as it is a determining factor for durability and biocompatibility of the prosthesis. Although in theory the synthetic materials have the potential to overcome problems associated with the mechanical and biological valves, to become a viable replacement option, the chosen polymer should not only have acceptable characteristics with regard to biostability, haemocompatibility, antithrombogenicity, resistance to degradation and calcification, but also good endothelial affinity. These strict criteria narrows the possible material choices for the heart valve apparatus (Burriesci et al., 2010). Among the most successful and popular materials for cardiovascular devices which has been studied since 1950s is polyurethane (PU). It has been testified that this polymer exhibits several characteristics important for this specific application due to its two-phase microstructure consisting of hard crystalline segments and soft elastomeric segments, the ratio of which determines some favourable properties, for example stiffness. Although PU might be perceived as an attractive material for heart valve prostheses, its main disadvantage associated with the long-term application is its biostability which is the result of its susceptibility to degradation. The degradation of polyurethane is caused by oxidation, acid hydrolysis or enzymatic pathways and leads to the loss of mechanical properties which in turn results in tearing and cracking of the leaflets. The second unfavourable factor is the calcification of PU leaflets which restricts its use in long term applications. In order to overcome those obstacles and improve the properties of PU prostheses, the changes in the soft segments of the polymers have been introduced as they have occurred to be the most vulnerable elements. Until now, the modification of soft segments led to three main types of polyurethanes: polyester urethane, polyether urethane and polycarbonate urethane which have been tested in biomedical applications. Among these three types of polyurethanes, the first to be used in medical devices was the polyester urethane, however it was quickly determined that because of its rapid hydrolysis of the polyester soft segments it is unsuitable for long term implantation devices. It was soon replaced by the polyether urethane which compared to polyester urethane has excellent hydrolytic stability, but some more

recent studies demonstrated that polyether is not free from unfavourable effect of oxidative degradation which leads to environmental stress cracking under in vivo conditions. Subsequently, the third generation of the polyurethanes – polycarbonate urethanes has been researched and found to have increased oxidative stability and significantly lower degree of biodegradation when comparing to polyether urethane (Ghanbari et al, 2009). Daebritz et al (2003) carried out the study where the durability of the mitral and aortic prostheses entirely made of polycarbonate urethane was tested in vitro and in vivo. In vitro fatigue testing was performed in testing facilities at 700 working cycles/minute, and the sample valves where examined once a week macroscopically for material degradation. In vivo testing was carried out on calves according to German guidelines for laboratory animal care during which the animals were subjected to mitral or aortic valve replacement through a left thoracotomy under general anaesthesia. In their experiment, it was proved through in vitro fatigue testing that the durability of the PCU mitral valves was between 600 million to 1 billion cycles, representing 15.8 to 26 years of normal human function what is in accordance to the requirements of the Food and Drug Administration (FDA) for mechanical heart valves (15 years). The PCU aortic valve test have proven to be durable for up to 450 million cycles, representing 11.8 years of normal function, and therefore satisfied the FDA requirements for biological heart valves (5 years). On the other hand, in vivo tests revealed that durability and haemodynamics were improved in those biological prostheses, and although the degeneration and calcification were mild for the mitral valve and moderate for the aortic valve, they still remained superior compared to bioprostheses. Finally, there was no increased thrombogenicity of the polymeric valves compared to biological valve prostheses (Daebritz, 2003).

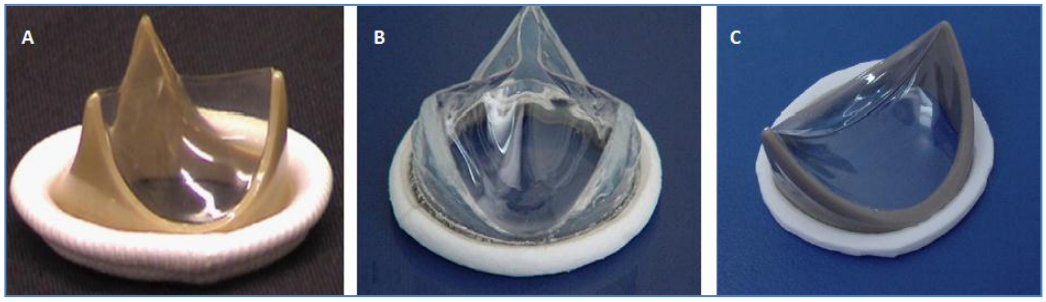


Figure 7. A: Polymeric heart valve with a frame machined from polyetheretherketone (PEEK) and coated with a thin layer of leaflet polyurethane. B: Trileaflet polyurethane valve. C: Bileaflet polyurethane valve (Zilla, 2008).

1.4 Valve design

Valve design is a challenging and complex procedure requiring visualisation and effective problem solving skills. Before starting the design process, certain performance criteria and the design parameters which satisfy those requirements must be identified. The necessary step is also evaluation of the structure of the ventriculoarterial valve in order to optimise the design and to provide maximum patient-valve match. All the valve design requirements were identified and reviewed below.

1.4.1 Arterial root

The evaluation of the structure of the ventriculoarterial valve is a crucial element in the design process as it provides information about the valve anatomy important for creating an optimised model. While evaluating the structure of the arterial valve, it is necessary to consider not only the leaflets but also features of the entire arterial root, whether aortic or pulmonary. The project involves designing the pulmonary valve, and therefore pulmonary root has been revised in this paper.

Pulmonary root is defined as part of the right ventricular outflow tract which supports the leaflets of the pulmonary valve. It is limited distally by the sintubular junction (Stamm MD, 1998). Its components include:

- The sinuses of Valsalva which are the 3 parts of the pulmonary root confined proximally by the semilunar attachments of the valvular leaflets and distally by the sinutubular junction. Based on the position to the aorta 3 different sinuses are distinguished: left-facing, right facing and non-facing.
- The valvular leaflets are inserted in the overall root of the tract, and they are attached in semilunar fashion, with the locus of attachment marking the haemodynamic ventriculoarterial junction. This line of attachment crosses the anatomic ventriculoarterial junction at six points. Thus, the leaflets arise in part from the infundibular musculature and in part from the arterial wall.
- The interleaflet triangles are the areas of the arterial wall proximal to the attachments of the leaflets which are incorporated within the ventricular cavity as a consequence of the semilunar nature of the attachments.
- The free standing distal right ventricular muscular infundibulum of the heart is the outflow portion of the right ventricle (RV). It is muscular over its entire circumference, forming a cylindrical sleeve that can be removed from the RV without encroaching the cavity of the left ventricle.

1.4.2 Design criteria

The valve design greatly influences the haemodynamic and structural performances of the valve, and can also help in meeting some of the surgical and manufacture specifications. Burriesci et al proposed the general requirements for an ideal artificial valve which need to be considered before design process. These requirements include haemodynamic, structural, biological, surgical and manufacture features.

Burriesci et al (2009) pointed out that one of the main haemodynamic valve requirements is a minimal resistance to forward flow which is related to the pressure drop needed to fully open the valve, and to the orifice area of the valve in its open configuration. The valve also should be designed in a way that provides minimal regurgitation in order to prevent large closing and leakage volumes. In addition, the effective design should minimise the loss of the ventricular energy what allows

prompter opening and closure. Finally, the valve should cause minimum damage to the blood cells as they are in constant contact, and do not cause thrombus formation.

When considering the structural requirements, it should be noted that the anatomy of the valve plays a very important role in its operative function by providing a competent and stable structure with specific anatomical and histological features. Although, it is difficult to create structure with an exact anatomy and functional features of a native valve, the structural design should aim to provide satisfactory hydrodynamic performance. The main structural requirement concerns the durability of the valve which according to FDA should be a minimum of 5 years for biological valves and 15 years for mechanical valves. Equally important is the longevity of the physical and geometric features providing that the individual elements will play their role without demonstrating the signs of wear or dehiscence.

With regard to the biological criteria, Burriesci et al (2009) pointed out that to provide satisfactory biological response, the artificial heart valve must be chemically inert with the human body and do not cause any damage to blood cells. Moreover, the tendency of vascular calcification should be kept at the lowest possible level to avoid the life-threatening stenosis caused by the calcium deposits. An ideal artificial valve would also simulate the healing process of the host tissues, provide good matching with the native anatomical site and not cause any discomfort to the patient.

While defining the surgical requirements, the possible delivery method is one of the important aspects that should be taken into account. The preferable method nowadays is minimally invasive approach that eliminates the risk factors that are present during the open heart surgeries. Therefore, many contemporary heart valves can be crimped without losing their original properties and deliver through the narrow arteries. However, no matter which method of delivery has been selected, it must be ensured that the chosen heart valve is suitable and will allow for a safe and satisfactory treatment. In reality there is no prosthesis that would last forever and all heart

valves have limited durability, therefore the ideal implant should be easy to replace, providing that the replacement procedure is minimally invasive in order to reduce the risk factors and the duration of treatment. Finally, due to anatomical and age differences of the patients, the heart valves should be available in a wide range of sizes so all patients can obtain optimal satisfactory treatment (Fleming, 2012).

The last group of criteria which an ideal artificial heart valve must comply with are manufacture features. Similarly to surgical requirements, properly and efficiently planned design process including the manufacturing aspects will further enhance and facilitate the whole procedure. Therefore, it is required that ideal heart valves are easy to manufacture, sterilise, store and transport to provide that at each of the stages, the medical product is of the highest quality. The design of the valve should also allow for the consistent repeatable manufacturing process as it has been shown that it might affect the durability and haemodynamic function of the valve. In the end, it should be provided that the final product is suitable for quality control procedures and is made to the highest standards.

Complying with all the criteria is a critical step in designing process as the goal of the procedure is to deliver the satisfactory product which will meet all the expectations of the physician and patient. Although, there is no ideal heart valve available on the medical market, it should be noted that it is important to optimise the elements of the designing process so the proposed valve strives to provide improved results compared to alternative options.

1.4.3 Material choice

The choice of leaflets material is a vital element in the design process of artificial heart valve as based on its properties it can be determined whether this particular material will comply with the design criteria for ideal valve prosthesis. While deciding which material will be used for developing valve prosthesis, it has to be considered whether it has acceptable characteristics with regard to biostability, haemocompatibility, antithrombogenicity, resistance to degradation and calcification, and

also endothelial cell affinity. Moreover, the proposed material should be flexible without affecting its durability in order to facilitate the method of heart valve delivery as well as its replacement. Finally, the material needs to be readily available and easy to manufacture. These essential properties significantly restrict the possible material choices for this application, and therefore put even more challenges on the researchers and physicians (Ghanbari, 2009).

In this paper, the main interest are the polymeric materials for heart valve prostheses as they represent an attractive alternative to the existing options, and therefore only materials that fall into this group have been investigated and discussed below. Among these materials are silicone, polytetrafluoroethylene (PTFE), polyurethanes: polyester urethane (PU), polycarbonate urethane (PCU), polyether urethane (PEU), polidymethylsiloxane – polyhexamethylene oxide polyurethane (PDMS-PHMO PU), polyvinyl alcohol, poly(styrene-block-isobutylene-block-styrene) (SIBS), and polyhedral oligomeric silsesquioxane – polycarbonate urethane nanocomposites (POSS-PCU).

Innovative researches in polymeric heart valve replacement in human were first reported in 1958. This was followed by a single trileaflet silicone rubber aortic valve implanted in several patients between 1960 and 1962. Nevertheless, a number of clinical trials carried out by this time were discontinued owing to the high occurrence of thromboembolic events. In 1960s, silicone was considered a material of choice due to its good flexibility and biocompatibility. However, again it was not free from several drawbacks. The formation of thrombosis as well as distortion and thickening of valve leaflets were observed during clinical investigations. Silicone heart valves suffered from structural failure, impaired haemodynamic performance and short durability, and was soon abandoned as a potential material for heart valve replacement (Kuan et al., 2011). Next material of choice became an expanded PTFE (ePTFE) owing to its good haemodynamic properties while applied in tricuspid valve prosthesis. After promising initial results, its leaflets were found to be prone to stiffening, free-edge inversion, calcification and stiffening. Application of ePTFE

heart valves was identified with high mortality rate due to leaflet rupture and thromboembolism, and it was decided that owing to several complications this material is not suitable for further development. The breakthrough came when Wiseman and colleagues invented a trileaflet valve fabricated from segmented polyurethane (SPU). The large central flow orifice of the leaflet valve similar to tissue valves reduces turbulence and blood trauma as a result of lower transvalvular pressure drop and better hydraulic efficiency. The valve has been found to have high flexure endurance, great strength and inherent non-thrombogenic characteristics (Kuan et al., 2011). The main types of PU which have been developed and tested are polyester urethane, polyether urethane and polycarbonate urethane. Although polyester urethane has been found to have good viscoelasticity, its main drawback appeared to be susceptibility to hydrolytic degradation. Unlike polyester urethane, the second generation of PU - PEUs were found to be characterised by good resistance to hydrolysis, however they appeared to be vulnerable to oxidative degradation and suffers from environmental stress cracking and metal ion oxidation under in vivo conditions. As a response to those two unsuccessful polyurethanes, PCU was introduced owing to its improved resistance to hydrolysis and oxidation. When compared to PEU, the biodegradation of PCU was significantly lower and limited to a thinner surface layer. Despite the satisfactory results with the third class of polyurethanes, it is not free from biodegradation and calcification in several in vitro and in vivo studies. To increase the biostability of PU, substitutions of its chemical structure have been made by linking the molecules which are resistant to biodegradation to the polymer. Incorporation of polidimethylsiloxane into the backbone of PU in the presence of polyhexamethylene oxide provides good thermal and oxidative stability. In addition, PDMS-PHMO PU was proven to have good mechanical properties and improved long-term stability. Nevertheless its main unfavourable feature is the difficulty of manufacturing process (Ghanbari, 2009).

In 2004, Jiang et al (2004) developed a one-piece tricuspid valve made entirely from polyvinyl alcohol cryogel (PVA-C). The mechanical properties of this valve demonstrated the significant reduction in flexural stresses of the leaflets. The stress con-

centrations at the commissural areas where the leaflets are attached to the stent were also avoided. Nevertheless, it has been pointed out that further studies are necessary to evaluate the potential of PVA-C valve as a superior material to current options. Lately, a novel polyolefin poly(styrene-b-isobutylene-b-styrene) (SIBS) was proposed as an outstanding polymeric material for heart valve application due to its good oxidation resistance. SIBS also demonstrated improved hemocompatibility and mechanical durability with over 350 million cycles evaluated in vitro. The polymer was found to be comparable to PU in platelet deposition tests, as well as tensile and fatigue properties after reinforcement of polypropylene fibres. Moreover, it has been noted that the platelet activation did not differ significantly from either a St. Jude bileaflet valve or a St. Jude Tissue valve. Such encouraging results have given the possibility of SIBS to become a potential material of choice with further development in polymeric heart valve prostheses (Kuan et al., 2011).

Another research carried out by Kidane and his colleagues (2009), it has been found that POSS-PCU nanocomposite might be characterised by excellent mechanical strength, good surface properties and resistance to platelet adhesion. It has been also shown that the material possesses comparable hardness and tear strength to commercially available products such as Estane or Chronoflex. Additionally, it has been pointed out that the hydrophobicity factor of the polymer helps resist the adsorption of blood proteins, which is necessary in preventing thrombosis and calcification on the heart valve surfaces (Kidane et al., 2009). Based on the potentially improved biocompatibility and biostability, the development of POSS-PCU nanocomposite heart valves is currently under further investigation.

Although several polymers have been proposed and investigated over the years, it is worth noticing that most of them are not free from harmful drawbacks or they require further investigation which would either confirm its safety or provide information on which properties of the material could adversely influence the performance of the valve. Therefore, as part of the design process all the advantages and disadvantages of the proposed material should be taken into consideration to evaluate the possible outcome when applying this particular material. The material

choice is very important in the development of the heart valve prosthesis as its characteristics must be in accordance with principles of designing process to provide an optimal treatment to the patients.

1.4.4 Surface modification

Another important aspect with regard to the material choice is its surface chemical and physical properties such as hydrophobicity, hydrophilicity and surface energy, as well as its morphology and topography. The importance of surface characteristics of the biomaterial is based on the fact they affect the interactions between the material and biological system which in turn will determine the material's biocompatibility. Although the recently developed polymeric materials present several advantageous properties, their interaction with biological systems can nevertheless be compromised by their surface characteristics. In order to improve some of the surface properties of the polymeric materials without changing their bulk properties, the surface modifications might be introduced. As one of the examples Ghanbari et al (2009) pointed out the possibility of improving cell attachment and proliferation on a synthetic surface by such techniques as plasma immersion ion implantation. In order to enhance the affinity of the surface to specific cell types such as endothelial cells, cholesterol and peptide modifications can be introduced. They realized that biofunctionalisation of the polymer surface can facilitate the attachment of the endothelial progenitor cells (EPCs) in the circulatory blood by providing cell-specific adhesion motifs on the surface of the synthetic biomaterial that promotes in situ endothelialisation (figure 8). Those two improvements play an important role as it has been shown that endothelialisation might protect the valve from being treated as a foreign body by the immune system, and also can facilitate the haemocompatbility of the surface.

Ghanbari et al (2009) also noted the importance of the topography of biomaterial surface emphasising that it affects several cell behaviours such as cell adhesion, proliferation, differentiation and apoptosis (figure 9). Although the underlying mechanisms of the resulting cellular response remain unclear, it is well known that

cells can sense and respond to the nanotopography of a material by so called 'contact guidance' which is a directed locomotory response of cells to an anisotropy of the environment. The example of such phenomenon is the tendency of fibroblasts to align along ridges or in parallel to the alignment of collagen fibres in a stretched gel. Therefore, introduction of a surface modification by creating specific topographic features at nanoscale might generate a 'cell-friendly' surface on polymers that are used in heart valve development. This might significantly enhance the biocompatibility and haemodynamic performance the valve prosthesis.

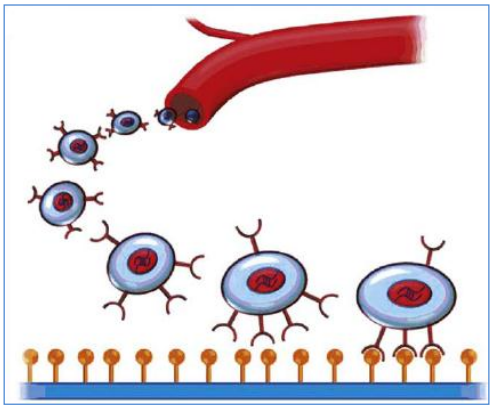


Figure 8. Schematic illustration presenting surface modification of synthetic material by biofunctional peptides. Biofunctionalisation of the polymer surface facilitates the attachment of EPCs in the blood by providing cell-specific adhesion on the surface of biomaterial (Ghanbari, 2009).

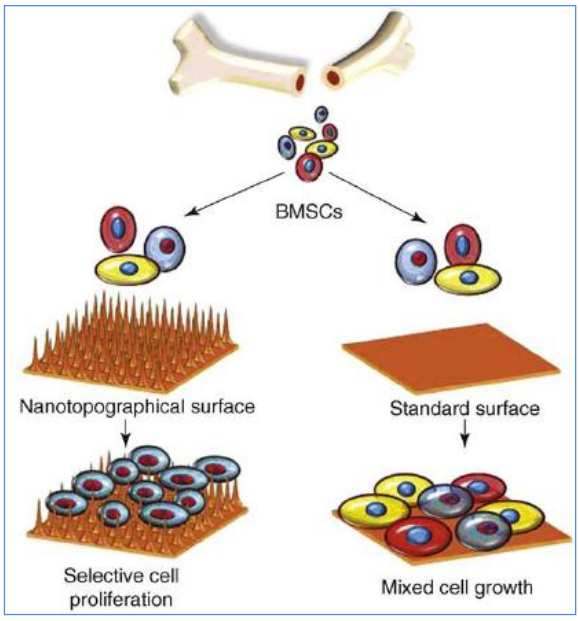


Figure 9. Schematic illustration presenting surface modification of synthetic material by nanotopographic features and compared with standard surfaces without any nanotopographical features. Surface topography might increase the affinity of the surface to a specific cell type, thus causing a selective cell proliferation (Ghanbari, 2009).

As it has been shown, the chemical and physical properties of the material's surface play a critical role in the design process of the heart valve prosthesis. Because of their influence on overall performance of the valve, the surface properties might be modified to improve such performance features as biocompatibility or haemodynamic functions.

1.4.5 Fabrication processes

The equally important role as choosing the most suited material for the design of the heart valve prosthesis plays the process of its fabrication. It is a critical element of the design process as the method of manufacturing might either favourably or adversely influence the properties of the final product, and therefore will determine if the valve is suitable for its application. For example, the manufacturing process might affect valve durability and haemodynamic function.

Several methods of polymeric heart valves such as dip casting, film fabrication, injection moulding and cavity moulding where investigated below.

Dip casting is a technique which involves the use of a specifically designed mandrel that undergoes repeated cycles of dipping in a polymer solution, and subsequent curing in air or dry air oven until the desired thickness is obtained. The final thickness of a dip-coated part depends on the viscosity of the bath, the rates of immersion and withdrawal, the temperature of the bath, and the number of dips. The concentration of the polymer solution varies depending on the polymer used and the stage of fabrication. Usually the process of dip casting involves multiple dips into a weak polymer solution. The major drawback of this method is the difficulty of controlling accurately the leaflets thickness distribution (Ghanbari, 2009).

During the film fabrication process, films of polymer are cast to the desired thickness. The leaflets are manufactured by cutting the film into the desired shape, and then by the use of solvent, the leaflets are bonded to the frame, which is fabricated separately. Finally, thermal forming is used to obtain the desired geometry of the valve.

Cavity moulding consists of a static assembly (female component) and moving assembly (male component), and is used to produce the whole structure of the valve by introducing hot polymer into the mould. Then, the sealed mould is introduced into a water bath, and subjected to alternate freezing and thawing cycle at -20°C and +20°C to form a thin film of polymer.

Injection moulding uses an injection moulding machine to fabricate the valve leaflets in the partially open position on a mandrel at injection pressure of 3500 atm and temperature of 110°C. Finally, hot and cold water baths are applied repeatedly to obtain the final valve (Ghanbari, 2009).

Ghanbari et al (2009), sum up several studies that have attempted to evaluate the impact of different fabrication methods on the function and durability of the obtained polymeric valves, and it was suggested that valves made by dip-casting process display better haemodynamic performance and durability than valves made by film fabrication methods. Nevertheless, it has to be noted that choosing appropriate fabrication method is limited by the polymer choice as some processes are not applicable for some specific types of polymers.

1.4.6 Construction of the valve

Another important step in the valve design procedure when certain performance criteria are established is determining the design parameters which would satisfy these criteria. With regard to principles of valve design, Thubrikar et al (1990) established the optimum performance criteria which are: (a) a certain minimum coaptation height, (b) no folds in the leaflet, (c) minimum valve height, and (d) minimum leaflet flexion. With such performance criteria, they described the design of the aortic valve (which anatomically is almost identical as the pulmonic valve) in terms of five parameters: radius of the base (Rb), radius of the commissures (Rc), valve height (H), height of the commissures (Hs), and the angle of the open leaflet to the vertical (β). Thurbikar et al (1990) pointed out that a valve described using these parameters has the following features:

- The leaflets are cylindrical
- The free edge of the open leaflet lies in a plane passing through the three commissures
- Part of the line of leaflet attachment is vertical (Hs)
- The remaining part of the leaflet attachment lies in a plane across which the leaflet can reflect to produce a closed valve.

Before the computer aided design, it is necessary to establish aforementioned parameters to construct an optimal heart valve model. In order to achieve this, it is required to gain knowledge on the anatomical dimensions of the human valve. Those values are critical in the construction process of the model as they will greatly influence the mechanical and structural properties of the prosthesis, and in turn will determine whether the proposed model is optimal for its application. Table 1 presents the design parameters of the aortic valve for the optimal valve, human valve and dog valve.

Table 1. Design parameters of the aortic valve with the radius of base 10 mm for optimal, human and dog valves (Thubrikar, 1990).

Valve	H (mm)	Rc (mm)	Hs (mm)	β (°)
Optimal valve	11.5	8-10	2.4 – 2.6	4 – 11
Human valve	14.2	10.0	7.1	0
Dog valve	11.7	8.3	5.0	5

Based on the dimensions of the human valve which is to be replaced by prosthesis, it is possible to evaluate the model parameters which would be able to take over the functions of the native valve and ensure they would stay unaffected. According to Thurbikar et al (1990) the absolute dimensions of the adult human aortic valve are Rb = 11.3 to 14 mm H = 15.7 to 19.8 mm, ϕ (the angle of the free edge to the

plane through the three commissures) = 25 to 37°, and α (the angle of the bottom surface of the leaflet to the plane through the three commissures) = 15 to 27°. They also demonstrated that changing only one design parameter is not enough to produce a better valve, and this change must be accompanied by changes in the other parameters. To optimise the performance of the heart valve model, they also specified the optimisation criteria which should be taken into account during design process. Thurbikar et al noted that it is desirable that Rc should be less than Rb. They explained that for any given β the valve height (H) is maximum when Rc = Rb. Therefore, as Rc decreases the H decreases meaning that reduction in Rc results in reduction of valve height. Nevertheless, it is important to state that too great reduction in Rc might produce an obstructive valve, allowing the commissures to project too far into bloodstream. In addition, they indicated that preferably β should be greater than 0° as for the positive value of β (1 - 10°), a valve with lower height can be obtained. They also observed that for the commissural height Hs = 0 only a very tall valve was possible, and for Hs = 1, 2 or 3 mm, a valve of greatly reduced height could be obtained. Hence, each of the design parameters Rc, β and Hs contributed to a reduction in valve height.

Thurbikar et al (1990) indicated that the three leaflet design is the most appropriate, and best suited for the normal aortic valve. For a valve located at the entrance of circular tubes, such as the aorta or pulmonary artery, the valve should produce a circular opening so that the blood flows smoothly. When the valve is open the circumference of the opening is $2\pi R$ where R is a radius of the circular opening, or $\approx 6R$. When the valve is closed the total length of the free-edges of the three leaflets is also approximately six times the radius. Hence, a three-leaflet valve can produce a circular opening without going through a large change in leaflet length. Another important factor while designing the leaflets of the valve is their thickness. Several researches were carried out on the performance of the heart valve with various thicknesses of the leaflets. For synthetic materials this value usually ranges between 100 μm to 300 μm. It has been found that leaflet thickness has a significant impact on the hydrodynamic performance of the heart valve prosthesis. Therefore, it is

necessary to provide that the leaflets with the proposed thickness parameter are able to resist residual stresses which are very likely to have a destructive impact on their durability, and also that the loss energy is kept at the possibly minimum level. The quantification of the energy loss parameter allows the assessment of both systolic and diastolic characteristics of the heart valves and provides information about the impact of valve function on myocardial performance (Akins et al., 2008).

While designing a model, it has to be understood that human heart valve in its natural functional state is always in motion. Although, it is helpful to consider the geometry of the static valve, it has to be noted that dynamic behaviour of the model should be also considered including four steps: (1) opening and closing of the valve, (2) motion of the various parts of valve, (3) design of the valve in vivo, and (4) high-speed studies of leaflet motion. Whereas the static design follows the principles of the overall design, the dynamic changes represent adaptation of this design to changes in the local environment. Thurbikar et al (1990) described the design of static valve model in terms of five geometric parameters, and they used five parameters as well to describe the dynamic state, but two of them were changed. The proposed parameters are radius of the base Rb, radius of the commissures Rc, valve height H, angle of the leaflet in the radial direction to horizontal α, and the angle of the leaflet free edge ϕ. In the dynamic valve design, α and ϕ replaced Hs and β respectively. The reason for choosing two different parameters is that they can be measured more accurately in vivo.

1.5 Design of the prototype of an expandable heart valve for paediatric deployment

Congenital heart disease is one of the most common types of birth defects, affecting up to 9 in every 1,000 babies born in the United Kingdom (NHS, 2014), as well it has been estimated that each year more than 4,000 new-borns are diagnosed with complex congenital heart diseases in the United States (Fleming, 2012). According to the statistics, it can be easily stated that the cardiac congenital defects are a serious problem. All the valvular pathologies in infants and children

pose several challenges to the paediatric cardiac surgeons. Repair of the heart valve remains the goal of the intervention due to its ability to restore valvular anatomy and physiology using native tissue, allowing for growth and potentially better long-term outcome. However, in many cases the reconstruction procedure fails or is not feasible, making the valve replacement the only possible choice of treatment. Nevertheless, the currently available prostheses for the replacement of affected heart valve in paediatrics present several disadvantages. Homograft and bioprostheses are characterised by superior haemodynamic results, but they are prone to accelerated degradation. The use of mechanical valves on the other hand is limited by the small patient size and the risk of thromboembolism. Another universal problem with all types of prostheses is the somatic outgrowth.

Because the available replacement heart valve options are not fully satisfactory, there is an open door for the alternative solutions which would be able to eliminate problem with short durability, and the necessity of chronic anticoagulation therapy.

It has been found that an ideal heart valve prosthesis for the paediatric deployment should not only comply with the general design criteria including haemodynamic, structural, biological, surgical and manufacture features, but also must be (Burriesci, 2010):

- Readily available in different sizes
- Associated with excellent durable haemodynamic profile
- Non – immunogenic
- Characterised by minimal thromboembolism risk, therefore eliminating the need of anticoagulation therapy
- Associated with excellent prosthesis longevity
- Characterised by low incidence of structural valve degeneration
- Must have growth potential proportional to somatic enlargement.

In 2012, two paediatric cardiac surgeons at Boston's Children Hospital (USA) – Sitaram Emani M.D. and Pedro del Nido M.D., have taken into consideration the main limitation of the available treatment options – fixed diameter and no possibility of

the valve to grow with a child, and decided to improve that. They came up with new solution by developing a replacement mitral valve that can expand as a child grows. For this purpose they used the Melody valve from Medtronic Inc., originally applied for the valve replacement in adults (Boston Children's Hospital, 2012). The Melody valve is a bovine jugular vein valve suture with a platinum iridium stent. It is an 18 mm valve that in the case of replacement in adult is crimped to 6mm and might be re-expanded from 18 to 22 mm (Fleming, 2012). Although the Melody is meant to be used at its full size, the surgeons noted that it still functions even when only partially expanded, enabling its application in children and infants. By trimming the length of the replacement valve and crimping it down to its smallest size, Emani has been able to implant it into five children at that time ranging from two months to six months old. He reported his team's experiences in a paper in the Annals of Thoracic Surgery. It has to be noted it was the first time the Melody valve has been used for mitral valve replacement.

The idea of the invention was very simple, but at the same time innovative. As the child grows, the modified valve was meant to expand by threading a thin balloon catheter into the heart, and carefully inflating it. Emani pointed out the further advantages of this procedure such as being less invasive than open heart surgery, and requiring less recovery time. The cardiac surgeons realised that potentially they could leave the modified valve in a proper position until a patient reaches adulthood, and in turn reduce the number of operations and the risk of lung swelling related to suboptimal valve function (Boston Children's Hospital, 2012).

In his paper Emani reported a case of a nine month old baby who had an irreparable mitral valve and which Emani's team replaced with a modified Melody prosthesis. Several months later, the team was able to successfully expand the prosthesis through a cardiac catheterisation procedure. They pointed out that compared to a major chest operation, a cardiac catheterisation procedure was much less invasive and required less recovery time (Boston Children's Hospital, 2012).

Quinonez et al (2013) also decided to examine the effectiveness of the Melody valve from Medtronic Inc. and reviewed in their paper the medical records of pa-

tients who had undergone Melody valve implantation in the mitral or left atrioventricular valve position from 2010 to 2013. In their study 11 patients had undergone implantation of the heart valve prosthesis at a median age of 7 months (range, 2-28). The techniques of valve modification and implantation included stent shortening, adding a pericardial sewing cuff, intraoperative balloon expansion, and fixation of the distal stent to the inferior left ventricle wall. They reported that the valve was competent, with a low gradient acutely postoperatively in all patients. However, one patient died, and one required permanent pacemaker implantation. In addition, one patient developed valve dysfunction and required removing an implant, whereas two patients without a pericardial sewing cuff developed paravalvular leaks. Finally, one patient who had not undergone distal stent fixation developed left ventricular outflow tract obstruction. Only three patients who had undergone subsequent catheter-based balloon expansion of the valve have continued to demonstrate acceptable valvular function. Based on their research, Quinonez et al. (2013) concluded that the Melody valve has demonstrated acceptable short-term function, however noted that the implantation techniques to prevent left ventricular outflow tract obstruction and paravalvular leaks should be considered. This indicated that Melody valve although successful in short-term therapy, still demonstrates several adverse effects and is not free from drawbacks. Although, the proposed solution seems to be an answer to fixed diameter prosthesis, it has to be noted that in terms of a long-term function valve's performance might not be as successful as in the case of short-term implantation. The main disadvantage of the proposed method is that although minimally invasive, it still requires several interventions as the valve needs to be expanded while the child grows. Therefore, an infant patient has to be subjected to the surgical procedures regularly until achieving adulthood to provide that diameter of the prosthetic valve suits the diameter of the native valve. Thus, while performing repeated cardiac catheterisation procedures there is an increased risk of adverse effects such as valvular leakage, rupture of the vessel, or the obstruction of the blood flow. The problematic issue can be also an examination of the somatic growth which has to be performed systematical-

ly and adequately so the patient obtains optimal treatment, i.e. the valve is expanded in the most suitable time without causing a threat to a patient's health. Finally, the effectiveness and safety of the modified Melody heart valve for the long term is still under investigation, and the other possible adverse outcomes can be met.

Based on the design criteria for the optimal heart valve implant, and by revising the possible solutions for the paediatric deployment, it can be stated that currently available options for the heart valve replacement in children and infants are limited and there is no optimal alternative for these prostheses. All of them demonstrated some significant drawbacks which can threaten the patient's life and be the reason of unsatisfactory treatment. Thus, there is still a great need for a development of the expandable heart valve prosthesis which would significantly reduce or even eliminate the problematic factors met while implanting the currently available options. Ideally, the proposed solution should be flexible to provide minimally invasive approach, associated with excellent durability and longevity, allowing the therapy free from anticoagulants, and finally what has not been achieved yet should have potential to grow proportionally to somatic enlargement. By taking into consideration the common problems and limitations of the contemporary heart valve implants in paediatrics, the new solution complying with this specified criteria has been proposed and presented in further chapters.

2. Objective and outline of the thesis

The objectives of the project can be specified as:

1) Establishing optimal design parameters for the development of the expandable heart valve for paediatric deployment.

2) Collecting data on Computational Fluid Dynamic model using the finite volume method in order to recommend the most suitable design.

3) Providing recommendation on the optimal material of choice which would comply with the design criteria for paediatric heart valve prosthesis with simultaneous indication of the project limitations, and suggestions in terms of further research.

The scope of the thesis included establishing design constraints such as valve height, commissural height, coaptation area, and design variables such as leaflets length and valve diameter. After deciding on the most suited parameters, nine different valves were created according to the design concept for a pulmonary valve, using CAD package Creo Parametric 2.0. The designed valves were divided into three groups according to the size of their diameter of the base: small, medium and large. For each type of the valves, three different heights of the valve were proposed and designed.

While having all nine valves developed, the designs were subjected to CFD modelling in order to simulate blood flow conditions through the pulmonary valve. This allowed for collecting data on local pressure, velocity and wall shear stress in order to analyse the performance of each valve. Based on the results, the most suitable valve for use as an expandable heart valve prosthesis for paediatric deployment was suggested.

3. Methodology

3.1 Concept development

An idea for the new valve prosthesis is to create an expandable heart valve which would offer the possibility of adjusting diameter of the prosthetic valve to the size of patient's native valve. Thus, the first step in the design process was establishing the concept of such heart valve prosthesis which would comply with the overall design criteria as well as the specific requirements for the paediatric deployment. For this purpose, the limitations of the currently available prostheses were revised and the alternative solutions were proposed. Based on the possible advantageous outcome, the final concept was recognised.

It was proposed that to achieve the expandable heart valve prosthesis, the material of choice needs to be flexible enough to allow for the changes in the diameter of the valve without compromising its original characteristics. However, not only the material plays the important role, but also the geometry of the valve. To allow the expansion of the prosthesis and to retain its optimal functions, the valve has been thought to be designed in a such fashion where the height of the prosthesis is adjusted for the application in adult, however to make the implantation possible in a child or infant, the radius of the base should fit the anatomy of a young patient. To achieve that, it was suggested to design a tall heart valve prosthesis with a small annulus. The idea for this design is that when the annulus would be expanded while the child grows, the leaflets would remain competent when changing their position with respect to the base of the valve as they are oversized and even when β increases, the edges of the leaflets still intersect each other. It means that when the valve closes and the leaflets move towards each other, their geometry and dimensions provide that the back flow of blood as it is pumped from the right ventricle to pulmonary artery is prevented.

Nevertheless, the decision on the most optimal dimensions for such application is quite challenging and selecting the parameters empirically can be problematic. It

was suggested that to identify the most suitable solution, three different radii of commissures and radii of base should be selected based on the anatomical dimensions available in the literature (Kaiser et al, 2008). It was proposed that they should represent three different groups: small, medium and large valves, so the differences in their performance can be easily identified. According to Thurbikar et al (1990) with regard to an aortic valve, the valve model to give an optimum performance should have minimum height. Choosing the valve which is too tall or too short can be connected with several adverse effects, and in real life could threaten patient's health. Therefore, it was recommended that for each type of the valve, three different height valves should be proposed. As a result nine different valve models were suggested so the optimal solution for an expandable heart valve prosthesis could be identified.

3.2 CAD modelling

In order to construct the leaflets of the pulmonary valve, Creo Parametric 2.0 was used. The first stage of construction involved designing the leaflets for three different sizes of valve in the fully open position. For this purpose, three design parameters were sufficient to establish – radius of base (Rb), radius of commissures (Rc), and height of the valve (H). To construct the upper edge of the leaflet, a circle of the previously specified radius of commissures was created. The edge of one leaflet was equal to 1/3 of the circle. To construct a bottom edge of the leaflet, the first step involved creating a plane parallel to the upper circle located a distal distance equal to established height of the valve. On the newly created plane, another circle of radius Rb was created, and divided into three parts corresponding to the upper edges. On the 1/3 of the second circle, a point being in the centre of both circles was created. The next step involved created a new plane passing through the entities of the upper edge of the leaflet and the point created on the bottom of 1/3 of the circle. By using a spline line going through the entities of the upper edge and the construction point of the bottom circle, the sketch of the valve leaflet was created

(figure 10). In order to obtain a 3D model, the leaflet was thickened, and the upper edges were rounded.

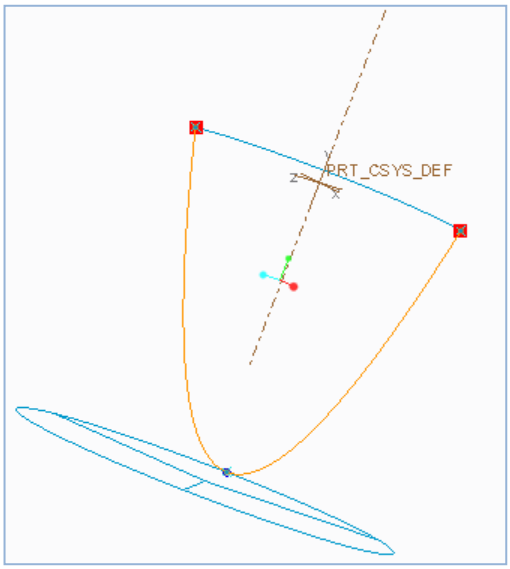


Figure 10. Schematic drawing to show the construction of the single leaflet. This particular leaflet was used to create a valve with large diameter of base, and the medium valve height.

To create symmetrical trileaflet model of the open valve, the design of the single leaflet was used to make an assembly around the central axis (figure 11).

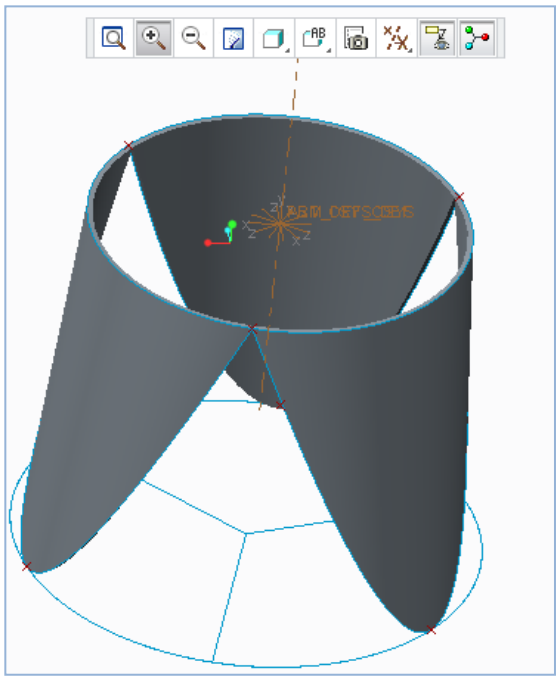


Figure 11. The leaflets design assembly as an example of an open valve model. The leaflets are coincident in the central axis, as well as the entities of each leaflet are coincident with the adjacent points.

To construct the closed valve, first of all the circle of the radius Rc was created and then divided into three symmetrical parts. The lines of the internal edge of 1/3 of

the circle were used to create the upper edge of the leaflet in the closed position. To give an appropriate shape of the upper edge of the leaflet, an arc was created at the point of the contact of two internal lines (figure 12).

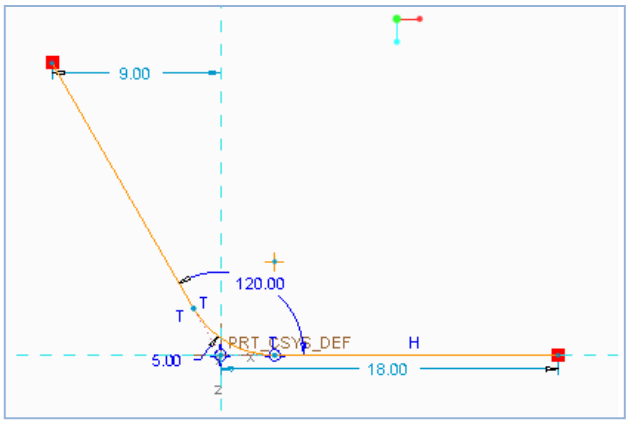


Figure 12. Schematic drawing of the construction of the upper edge of the leaflet.

In the plane located at a distance equal to the proposed height of the valve, a circle of radius Rb was created which was then divided into three symmetric parts. On the outer edge of the 1/3 of the circle, a point passing through the centre of the line was constructed. Then, the entities of the upper edge of the leaflet were connected with the centre point of the bottom line through the spline function to apply shape of the leaflet. Finally, the construction was thickened and the edges were rounded (figure 13). To make an assembly, three leaflets were joined together by making the axis and the entities of the upper edged coincident (figure 14).

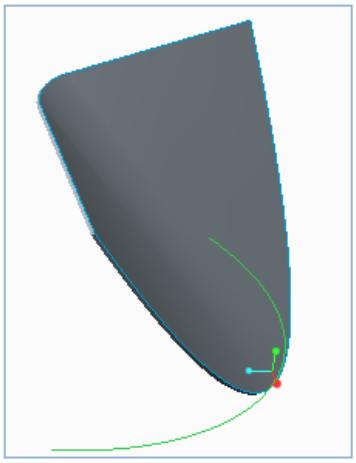


Figure 13. The design of the single leaflet in a closed position (left).

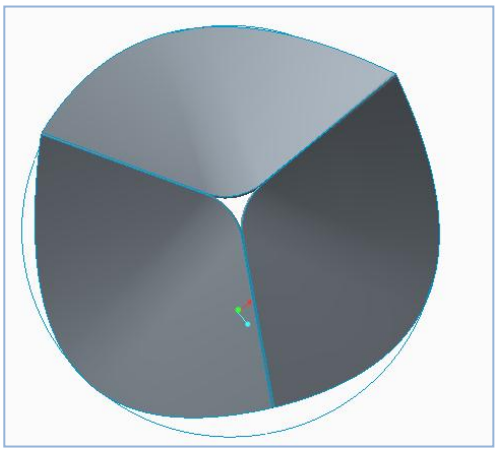


Figure 14. The leaflets assembly design as an example of closed valve model (right).

For the purpose of fluid-solid interaction, the solid pipe (cylinder) of the radius equal to Rb was created for each model of the valve to mimic the function of the pulmonary artery, and to give the boundary to the blood flow. Pipes and leaflets were assembled together by making the axis of the valve and the pipe coincident, and by ensuring that the leaflets are placed on the bottom surface of the pipe. After assembling these two elements, the leaflets were cut out from the pipe and the model was saved as a STEP file, suitable for the CFD simulation in Ansys Workbench.

3.3 FVM modelling

Finite Volume Method modelling can be easily performed using Ansys Workbench 15.0 platform. Ansys Workbench includes Ansys Fluent software which is a specialised tool for solving complex fluid problems. For the purpose of the project, the simulation of the steady blood flow through the pulmonary valve was performed.

FVM modelling included the following steps (figure 15):

- Updating model geometry
- Mesh generation
- Setting up the suitable boundary conditions for the blood flow through pulmonary conduit and valve

- Running the solution
- Displaying and analysis of the results for pressure, velocity and wall shear stress.

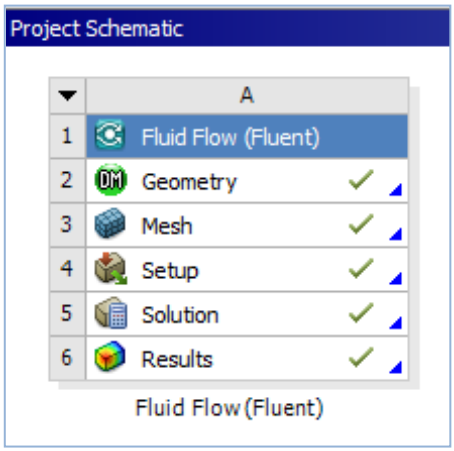


Figure 15. Project schematic including all necessary steps to complete the simulation.

After transferring the CAD file into Ansys Workbench, the meshing was carried out using linear tetrahedral elements (figure 16). The aim of the mesh generation techniques is to divide complex problems into small elements. The tetrahedral mesh starts from a 3D boundary mesh containing only triangular faces and generates a mesh consisting of tetrahedral elements. The importance of the mesh can be easily explained by the fact it influences the accuracy, convergence and speed of the solution. The time it takes to create and mesh a model is often a significant portion of the time it takes to get results from a computer aided engineering solution. While choosing the technique, one needs to be aware that with the finer mesh, the solution is more precise, but it requires more time for processing. Therefore it is recommended to achieve balance between mesh density and processing time.

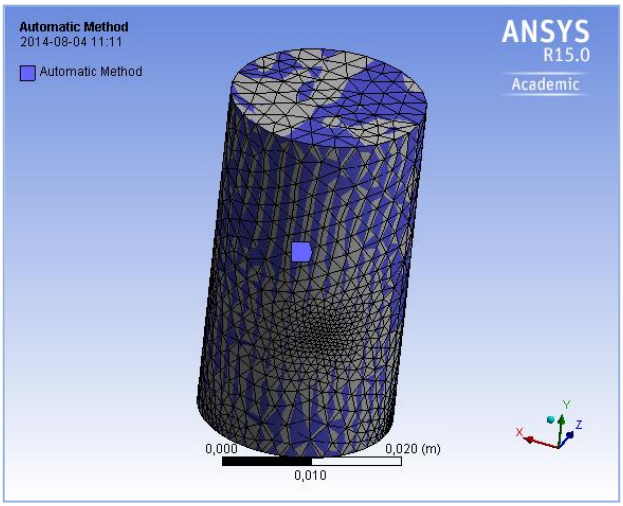


Figure 16. An example of meshing generation technique with the automatic method applied.

In order to simulate the flow of blood through the valve leaflets, the model fluid was changed to blood with a constant density of 1060 kg/m^3, and a constant viscosity of 0.0034 kg/ms. The next step included creating suitable parameters at the inlet and outlet of the pipe which would mimic the normal conditions in the pulmonary artery. The inlet parameters included the average velocity magnitude which was set up as 0.75 m/s (according to mean velocity of the blood through the pulmonary artery), and the X, Y and Z velocity components where X and Z were equal to 0, and Y was changed to 1. The outlet parameter – gauge pressure was set to 15 mmHg according to the average blood pressure value in the pulmonary artery. A steady pressure-based segregated solver was used with a second order discretization scheme chosen for the pressure equations, and a second order upwind scheme chosen for the momentum equations. The flow field was initialized using the initial values computed from the input boundary conditions.

After obtaining the X, Y, Z velocity calculations, the results for local pressure, velocity and wall shear stress distribution were displayed. For the graphical representation of pressure and velocity distribution, an XY plane was created passing through the center of the pipe which enabled visualization of the pressure and velocity magnitudes through the pipe. The wall shear stresses distribution was presented on the wall of the pipe and the leaflets.

All the results obtained during the simulations were presented in next chapter.

3.4 Material choice for an expandable heart valve

The last process in a complex procedure of designing the heart valve prosthesis for the expandable valve model for pediatric deployment is deciding on the most suitable material which would comply with the design criteria for this specific application. With regard to the literature on current solutions and by studying their limitations, the new alternative was suggested. The detailed description of the proposed approach including shape memory polymers and their application in heart valves can be found in chapter 5

4. Results

4.1 CAD models of the pulmonary valve for paediatric deployment

a) Dimensions of the heart valve models

The designing process involved creating nine different valves suitable for paediatric deployment. Among these nine heart valve models, three groups were distinguished: small valves (SV), medium valves (MV) and large valves (LV). For each type of valve such parameters as radius of base, radius of commissures and thickness of leaflets was kept constant. The only changing variable was the height of the valve in order to investigate the influence of this parameter on the performance of the valve. All the dimensions of the designed models are presented below in table 2.

Table 2. Design parameters necessary to create models of the pulmonary valve. All dimensions are presented in millimetres.

Valve	Radius of the base (Rb)	Radius of the commissures (Rc)	Height of the valve (H)	Thickness of the leaflets
SV1	7	5	16	0.25
SV2	7	5	17.5	0.25
SV3	7	5	19	0.25
MV1	9	7	16	0.25

MV2	9	7	17.5	0.25
MV3	9	7	19	0.25
LV1	11	9	16	0.25
LV2	11	9	17.5	0.25
LV3	11	9	19	0.25

According to Thurbikar et al (1990) who stated that the angle of the open leaflet to the base β should be between 1 and 10°, the dimensions provided above were chosen based on these assumption. Therefore, before deciding on the parameters for the optimal design process, β was calculated to ensure that for each type of valve the angle has the approximate dimension. The example calculations are presented below.

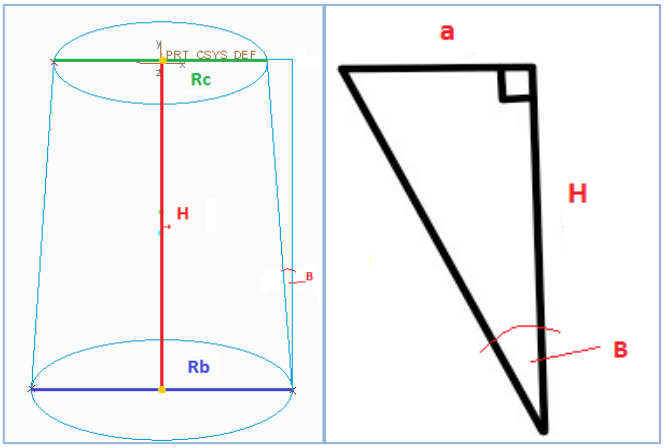


Figure 17. Schematic drawing of the geometry of the valve leaflets in the fully open position presenting Rb, Rc, H and β. β can be calculated according to the trigonemetric functions as *a* and H are known dimensions.

To calculate the angle β, the first step should be identifying *a* by knowing it is equal to the difference between Rb and Rc. For all valves this difference was kept constant and was found to be 1.5 mm. By knowing the height of each valve, β can be calculated by applying trigonometric rules:

Equation 1. $\beta = \tan^{-1}(a/H)$

As *a* is a constant value when the height is unchanged as well, the angle of the open leaflet to the base is identical although the radius of commissures and radius of the base are different for each type of valve. For the proposed models, β is between 6-7 °. β values were found for each type of valve and presented in the table below (table 3).

Table 3. **The angle of the open leaflet to the base β for each type of the valve. (SV1 – small valve 1, MV1 – medium valve 1, LV1 – large valve 1 etc).**

Valve	SV1	SV2	SV3	MV1	MV2	MV3	LV1	LV2	LV3
β	7	6.5	6	7	6.5	6	7	6.5	6

b) Heart valve models

After determining the optimal dimensions of the valve prostheses for the paediatric deployment, the valve models were designed in Creo Parametric 2.0. The design was completed according to the method described in chapter 3. Examples of the heart valve models for a fully open are presented below.

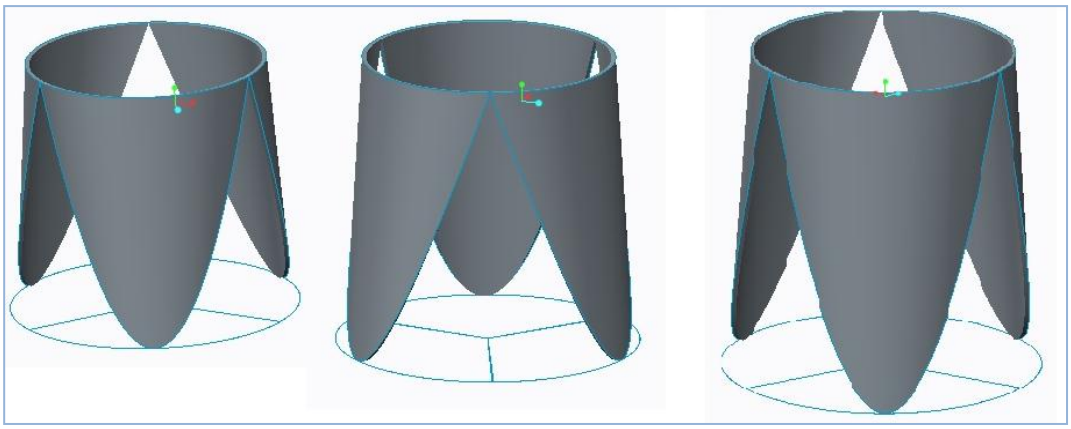


Figure 18. Example of three designs of the leaflets with the same radii of base and radii of commissures , but with different height of the valve. Starting from the left: MV1, MV 2, MV3. Valves with the same Rb and Rc, but different H were used in simulation in order to identify the influence of height of the valve on the pattern of blood flow through pulmonary conduit.

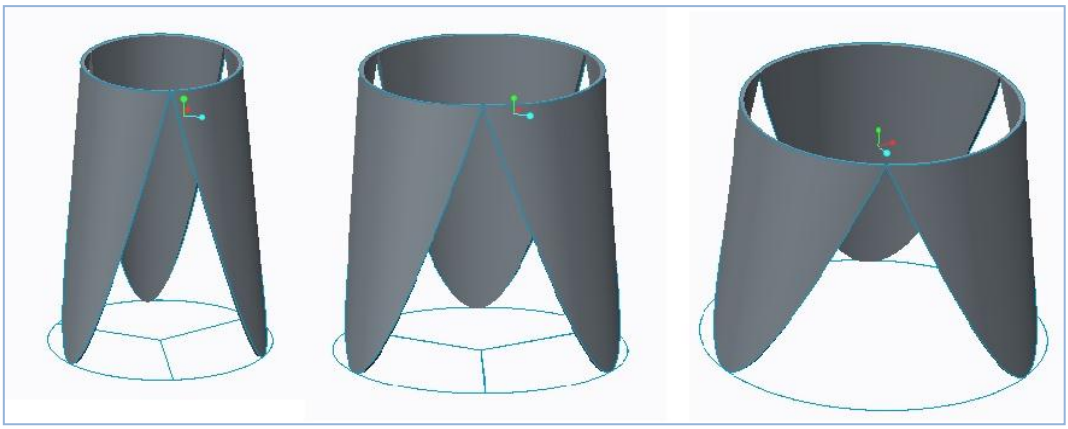


Figure 19. Example of three designs of the leaflets with different radii of base and radii of commissures and different height of the valve. Starting from the left: SV3, MV2, LV1.

When designing the leaflets in a closed position, the dimensions Rb, Rc and H were constant, however the position of the leaflets with respect to the base of valve has changed. The leaflets were allowed to intersect each other to mimic the anatomy and the function of the pulmonary valve in a closed position. An example of the design of the leaflets in the closed valve is presented in figure 20.

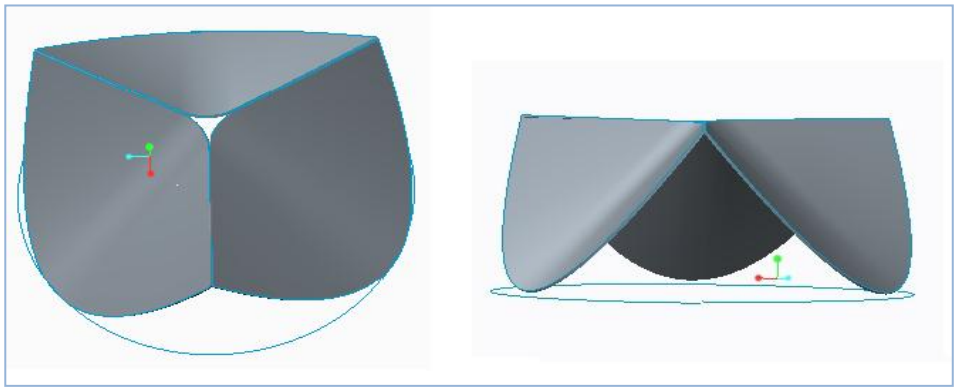


Figure 20. Valve design with the leaflets in a closed position. Letf: valve seen from the top. Right: valve seen from the front. The above model presents medium valve with the height equal 16 mm.

For the purpose of the FVM simulation, the pipe mimicking the pulmonary conduit was designed. Each cylindrical solid pipe was created in a fashion where the radius of the pipe was equal to the valve's radius of the base. For ach valve the height of the pipe was constant and equal to 45 mm. To conduct the simulation the leaflets and the pipe were assembled in a fashion described in section 3.2. The example of the design of the pulmonary conduit is presented in figure 21.

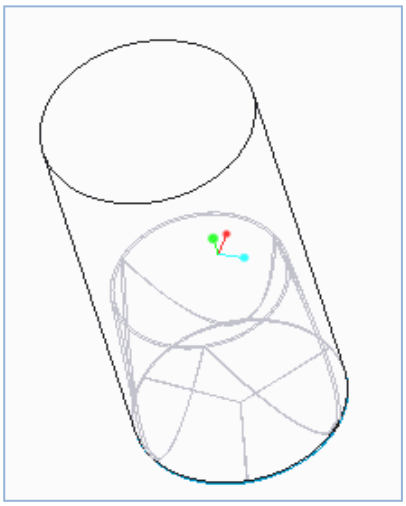


Figure 21. Schematic drawing of the pipe as the pulmonary conduit with the leaflets attached inside the structure and cut out from the model for purpose of the FVM simulation.

4.2 FVM simulation results

FVM modelling was carried out for each valve to analyse the pressure distribution, the velocity and wall shear stresses that occur within the valve when the blood flows through it. A Newtonian model of blood flow was chosen for this purpose. The condition parameters for the blood flow such as blood viscosity, blood density, arterial pressure and velocity were presented in the table below (table 4).

Table 4. Blood model parameters used in FVM simulation.

Blood viscosity [kg/ms]	1060
Blood density [kg/m^3]	0.0034
Mean blood velocity (pulmonary artery) [m/s]	0.75
Mean arterial pressure (normal pulmonary artery) [mmHg]	≈15

a) Mesh generation

As a part of the FVM modelling, the meshing generation was introduced in order to divide the geometry of the model into small elements. The method of meshing used in this simulation provided the tetrahedral elements. Examples of meshed models

are presented in figures 22, 23 and 24 where the meshing technique was introduced on SV1, MV1 and LV1.

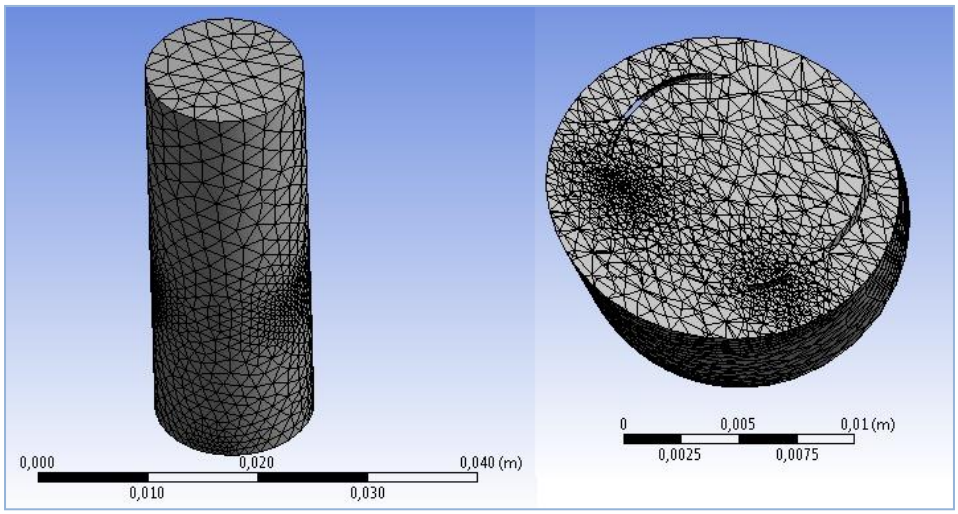


Figure 22. Example of mesh generation technique. On the right - Mesh generation on the geometry of the pipe and small valve 1 assembly. On the left – mesh presented through the cross section of the model.

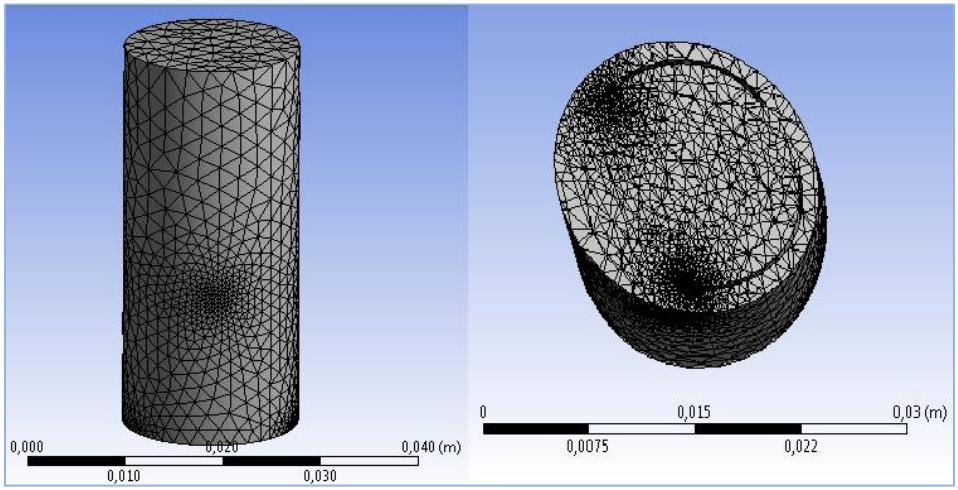


Figure 23. Example of mesh generation technique. On the right - Mesh generation on the geometry of the pipe and medium valve 1 assembly. On the left – mesh presented through the cross section of the model.

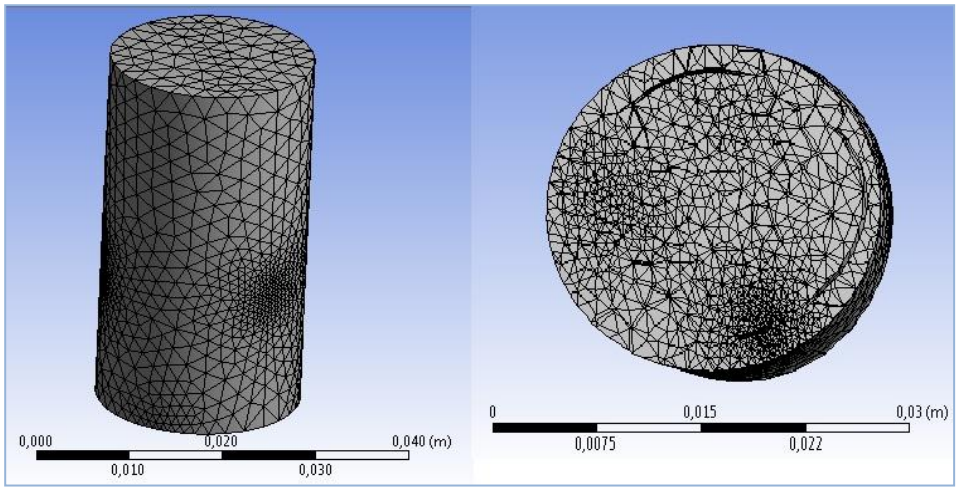


Figure 24. Example of mesh generation technique. On the right - Mesh generation on the geometry of the pipe and large valve 1 assembly. On the left – mesh presented through the cross section of the model.

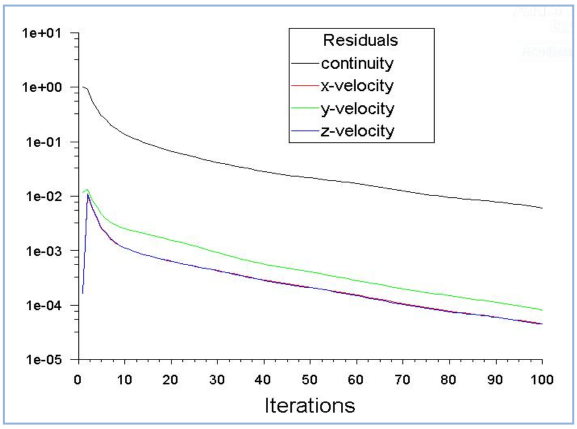
The results on the volume of each model, and number of nodes and tetrahedral elements created through mesh generation are presented in table 5.

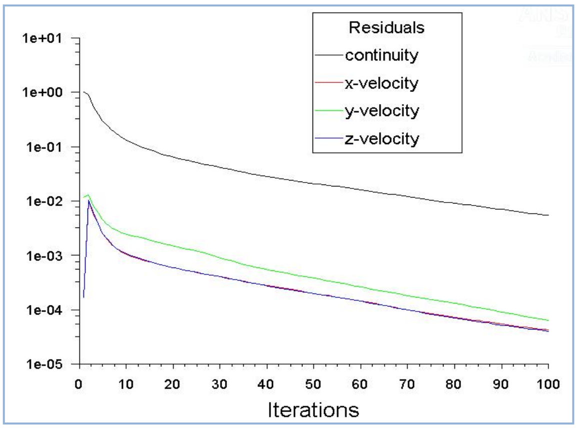
Table 5. Table presenting volume of the geometry, number of tetrahedral elements and number of nodes generated during meshing method for the purpose of FVM simulation.

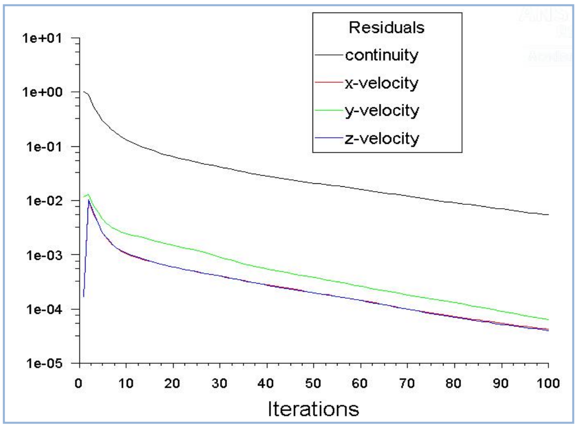
Valve	Geometry volume [m^3]	No. elements	No. nodes
SV1	6.529×10^{-6}	143 817	26 145
SV2	6.5218×10^{-6}	142 008	25 816
SV3	6.5148×10^{-6}	140 544	25 594
MV1	1.0064×10^{-5}	144 863	26 310
MV2	1.0053×10^{-5}	143 500	26 097
MV3	1.0043×10^{-5}	143 032	26 091
LV1	1.5066×10^{-5}	158 801	28 604
LV2	1.5054×10^{-5}	154 273	27 840
LV3	1.5041×10^{-5}	154 804	27 967

b) X, Y, and Z velocity components calculations

Once completing mesh generation and setting up the optimal boundary conditions for the blood flow through pulmonary conduit and valve, the X, Y and Z velocity components were calculated and plotted. The examples of the resulting solutions are presented in the graphs below.







Plot 1, 2 and 3. The above plots present the X, Y and Z velocity components calculated for small valve 1, small valve 2 and small valve 3 respectively.

c) Pressure distribution

After completing the calculations of the velocity components, the pressure results were displayed presenting the distribution and the values for the XY plane passing through the model of the pulmonary conduit, and for the wall of the pipe. The scales were equalised for comparison.

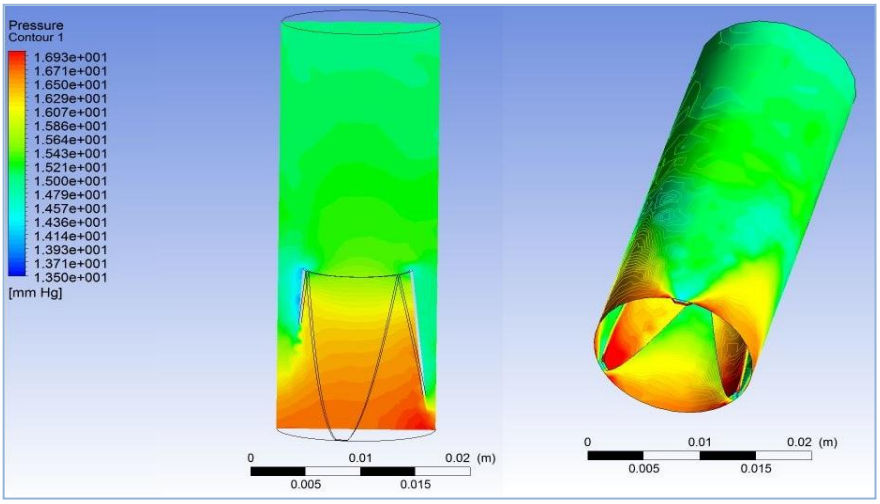


Figure 25. Graphical presentation of the pressure distribution in the pulmonary conduit with the small valve 1.

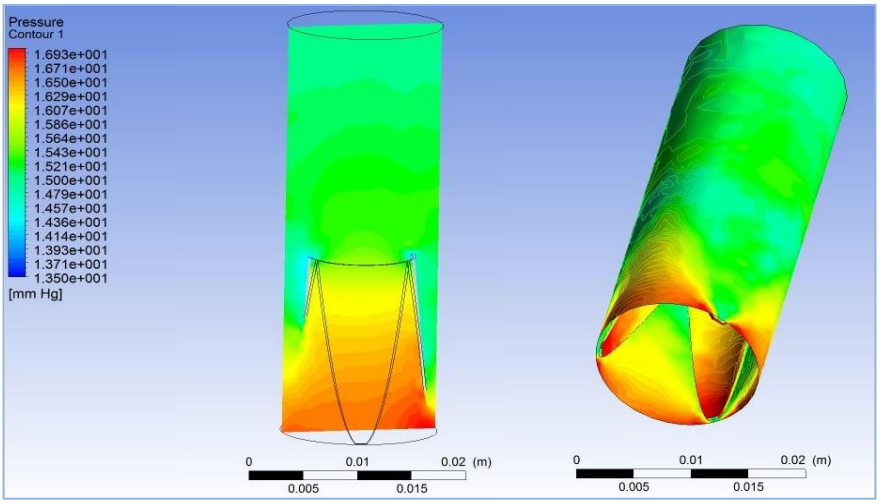


Figure 26. Graphical presentation of the pressure distribution in the pulmonary conduit with the small valve 2.

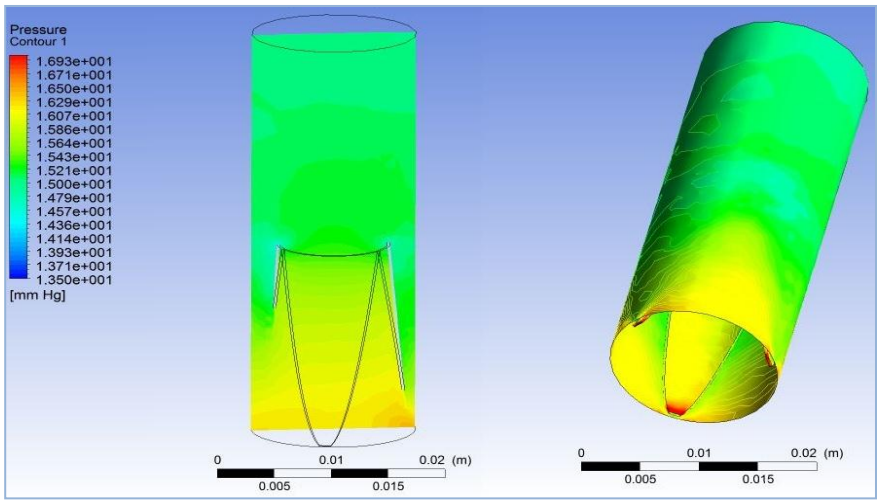


Figure 27. Graphical presentation of the pressure distribution in the pulmonary conduit with the small valve 3.

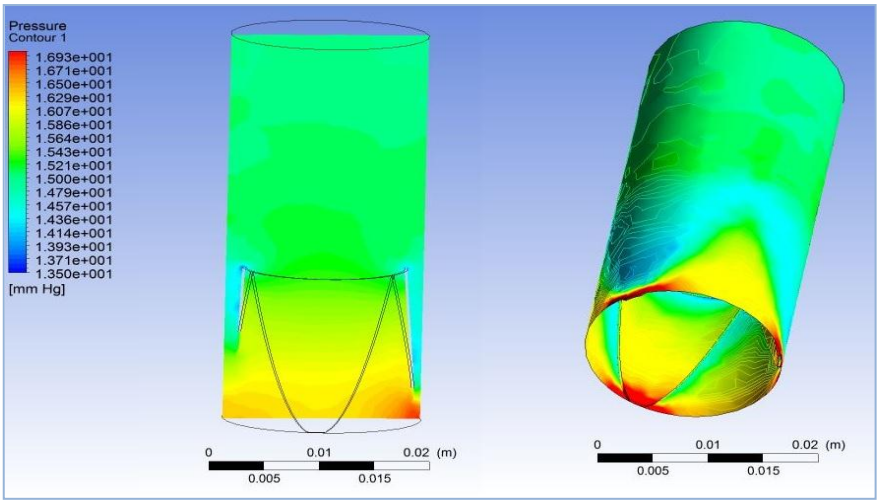


Figure 28. Graphical presentation of the pressure distribution in the pulmonary conduit with the medium valve 1.

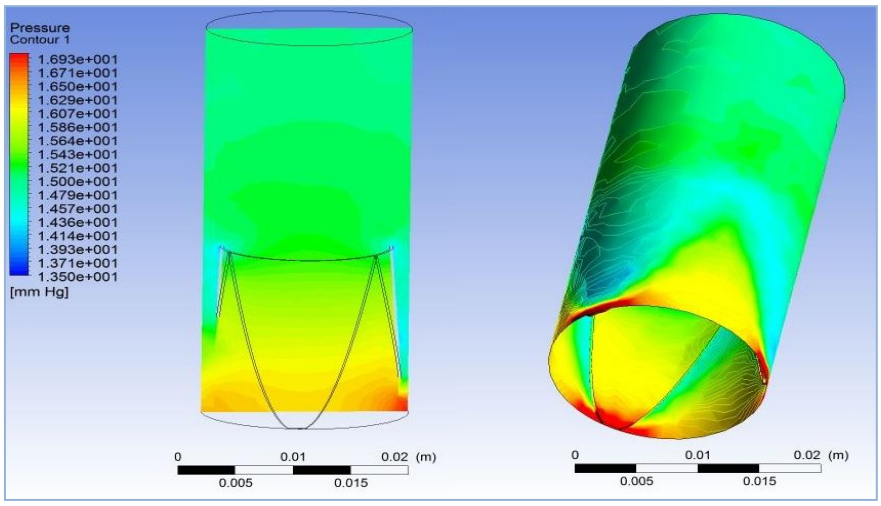


Figure 29. Graphical presentation of the pressure distribution in the pulmonary conduit with the medium valve 2.

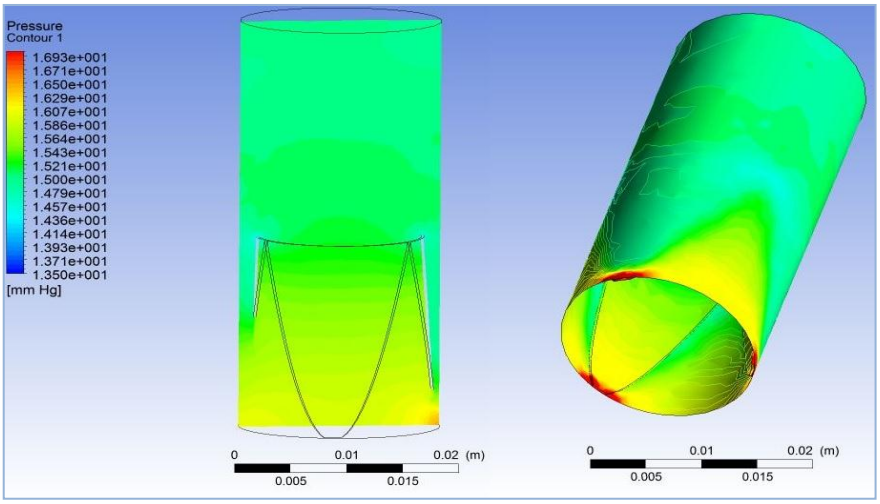


Figure 30. Graphical presentation of the pressure distribution in the pulmonary conduit with the medium valve 3.

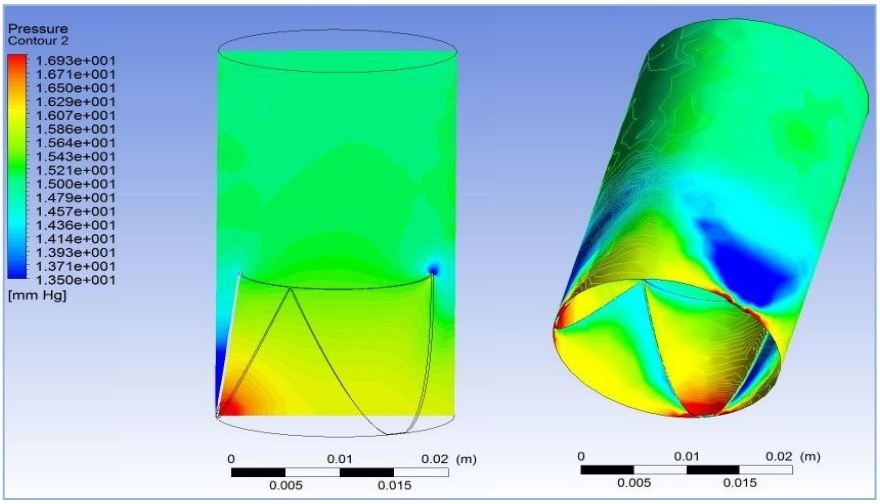


Figure 31. Graphical presentation of the pressure distribution in the pulmonary conduit with the large valve 1.

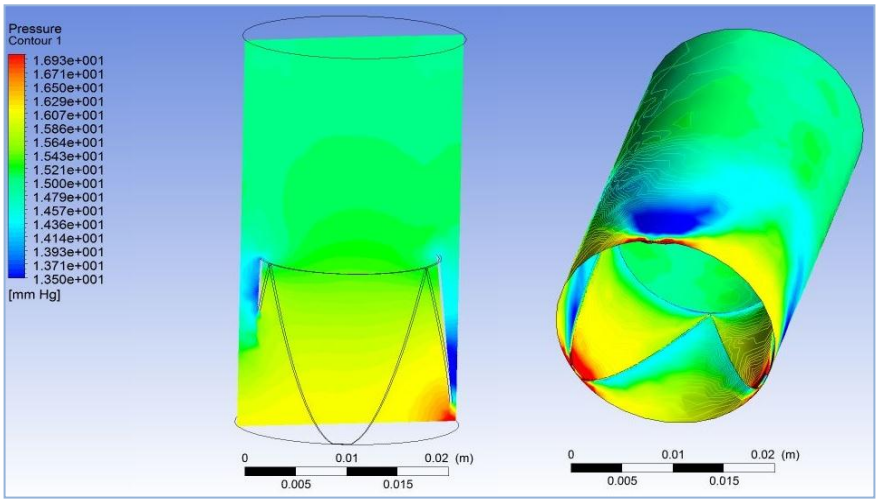


Figure 32. Graphical presentation of the pressure distribution in the pulmonary conduit with the large valve 2.

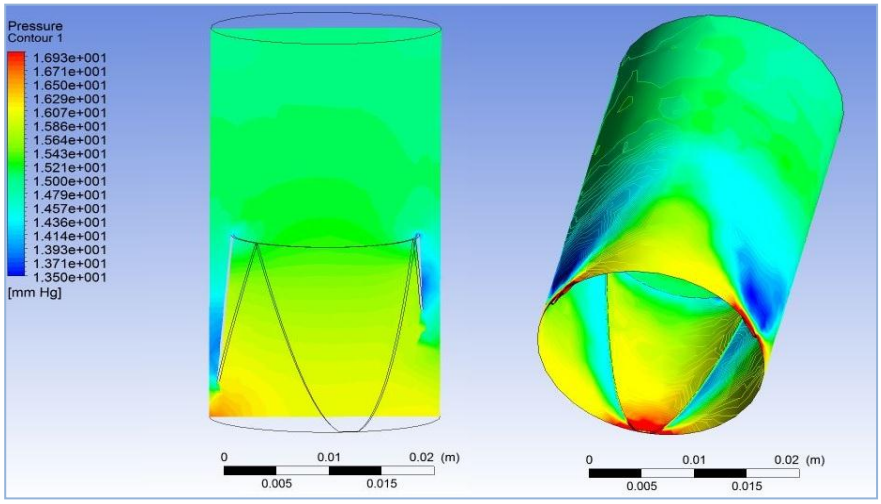


Figure 33. Graphical presentation of the pressure distribution in the pulmonary conduit with the large valve 3.

d) Velocity distribution

Velocity results were displayed below presenting the distribution and the values in the XY plane passing through the model of the pulmonary conduit. The scales were equalised for comparison.

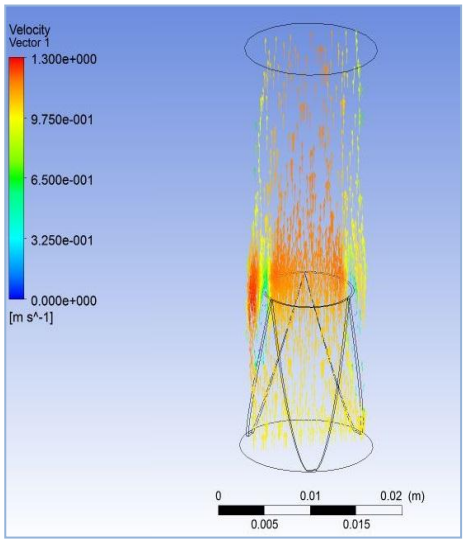


Figure 34. Graphical presentation of the velocity distribution in the pulmonary conduit with the small valve 1.

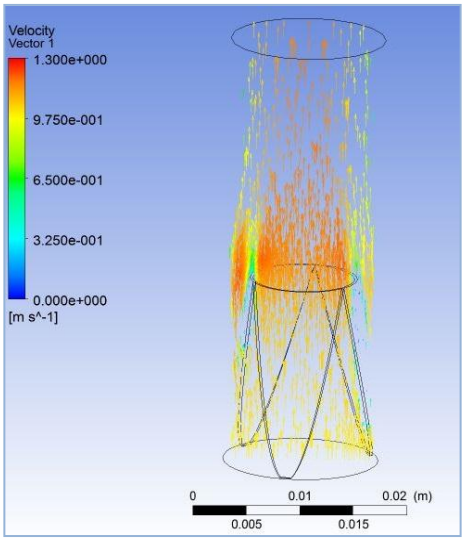


Figure 35. Graphical presentation of the velocity distribution in the pulmonary conduit with the small valve 2.

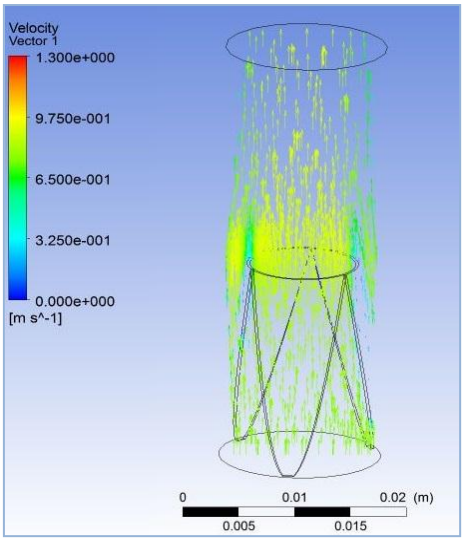


Figure 36. Graphical presentation of the velocity distribution in the pulmonary conduit with the small valve 3

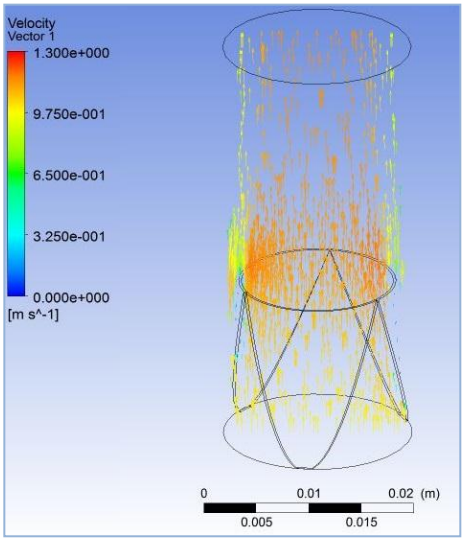


Figure 37. Graphical presentation of the velocity distribution in the pulmonary conduit with the medium valve 1.

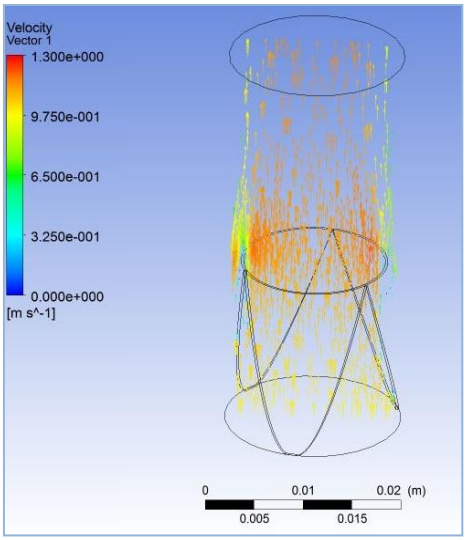


Figure 38. Graphical presentation of the velocity distribution in the pulmonary conduit with the medium valve 2.

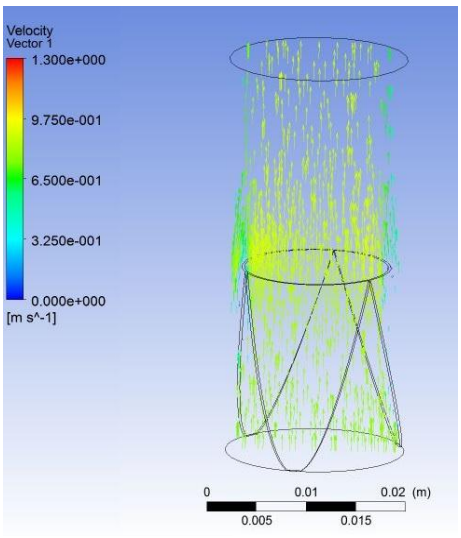


Figure 39. Graphical presentation of the pressure distribution in the pulmonary conduit with the medium valve 3.

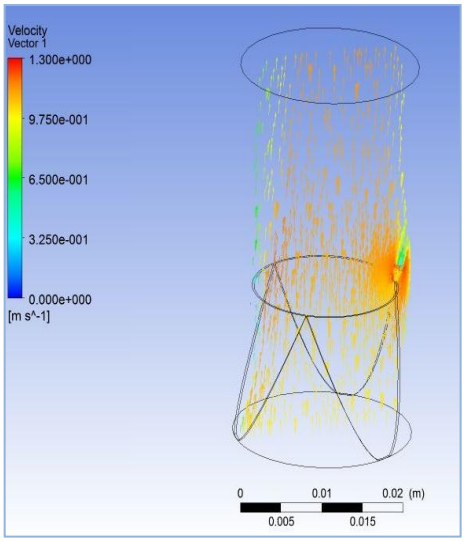


Figure 40. Graphical presentation of the pressure distribution in the pulmonary conduit with the large valve 1.

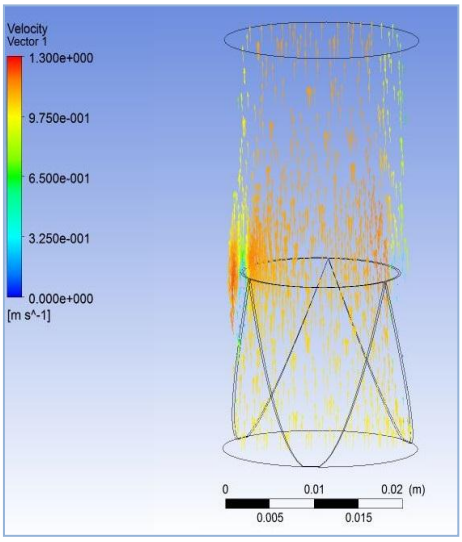


Figure 41. Graphical presentation of the pressure distribution in the pulmonary conduit with the large valve 2.

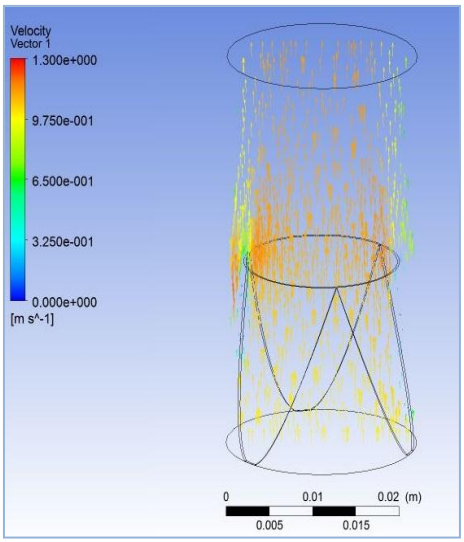


Figure 42. Graphical presentation of the pressure distribution in the pulmonary conduit with the large valve 3.

e) Wall shear stress distribution

The results of wall shear stress distribution on the wall of the pulmonary conduit model were displayed as a part of the simulation and are presented below. The scales were equalized for comparison.

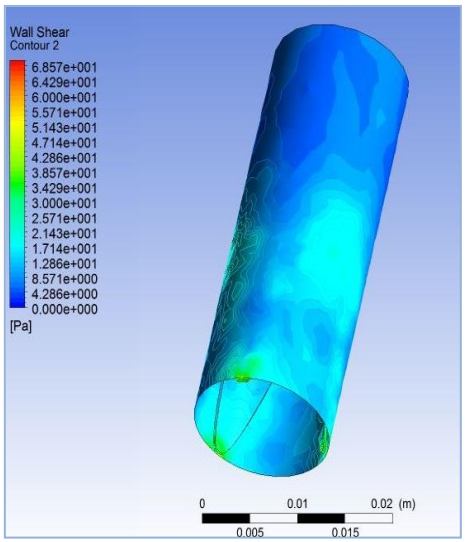


Figure 43. Graphical presentation of wall shear stresses present at the pulmonary conduit and small valve 1.

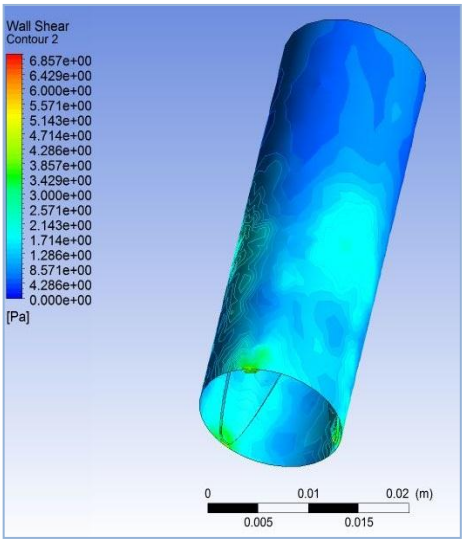


Figure 44. Graphical presentation of wall shear stresses present at the pulmonary conduit and small valve 2.

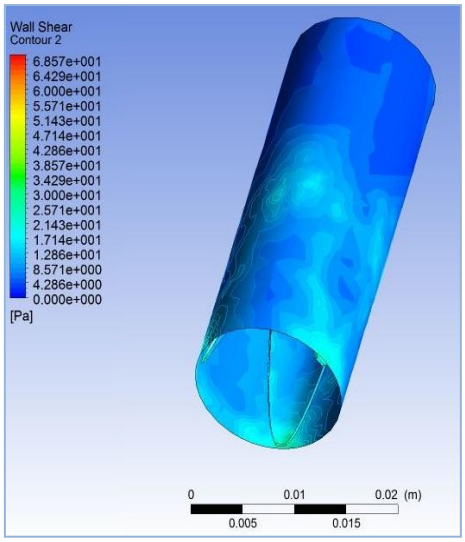


Figure 45. Graphical presentation of wall shear stresses present at the pulmonary conduit and small valve 3.

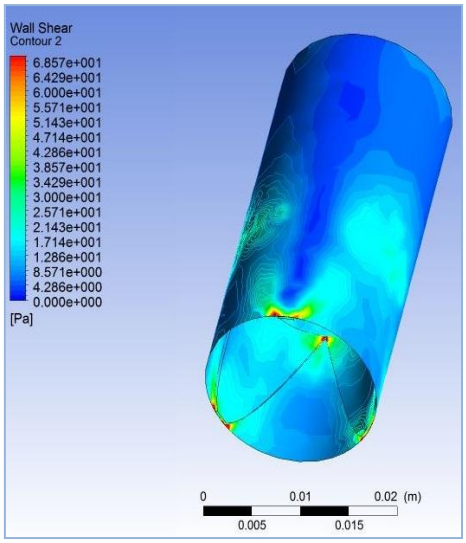


Figure 46. Graphical presentation of wall shear stresses present.

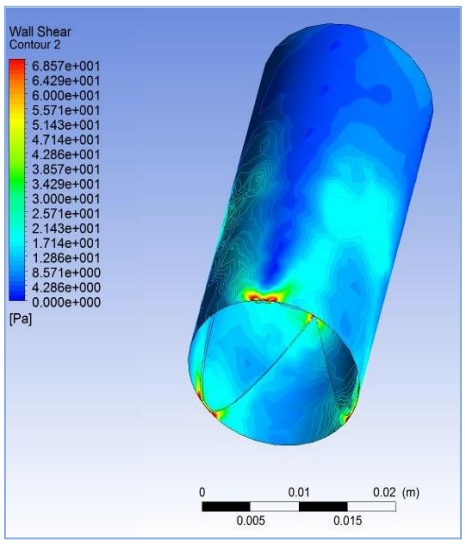


Figure 47. Graphical presentation of wall shear stresses present at the pulmonary conduit and medium valve 2.

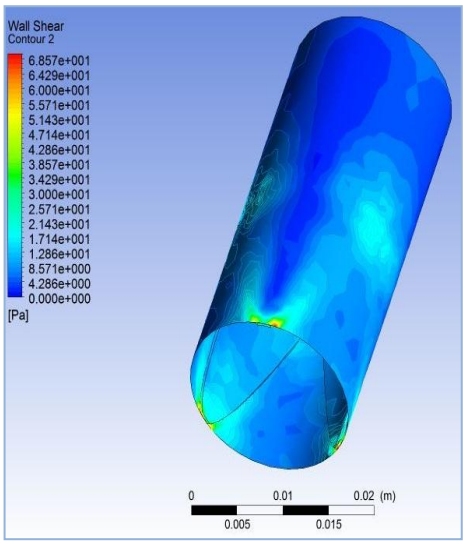


Figure 48. Graphical presentation of wall shear stresses present at the pulmonary conduit and medium valve 3.

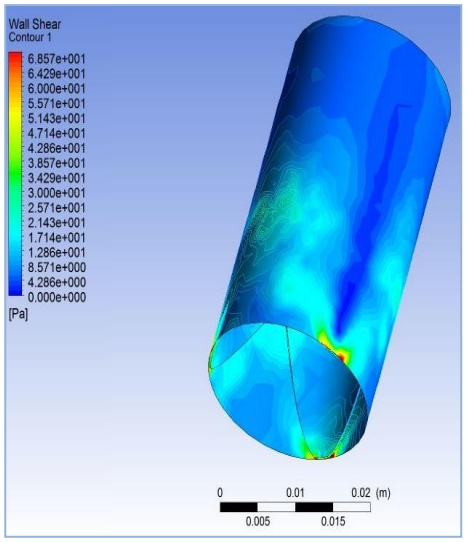


Figure 49. Graphical presentation of wall shear stresses present at the pulmonary conduit and large valve 1.

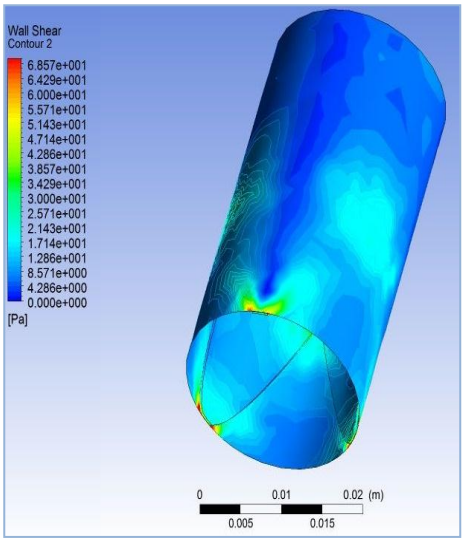


Figure 50. Graphical presentation of wall shear stresses present at the pulmonary conduit and large valve 2.

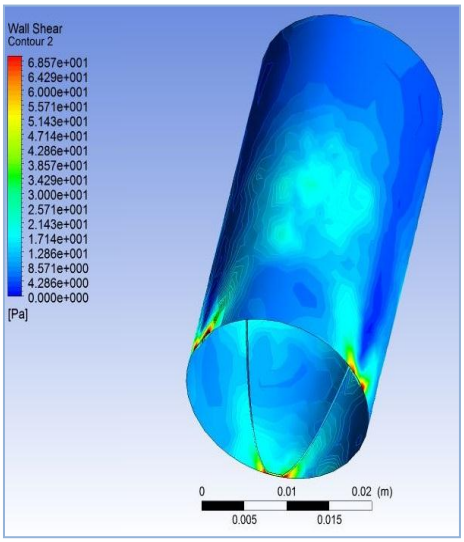


Figure 51. Graphical presentation of wall shear stresses present at the pulmonary conduit and large valve 3.

5. Discussion of the results

During this research, it has been recognised that currently available options for the heart valve prostheses in the paediatric deployment present several drawbacks. The mechanical valves despite the superior durability require lifelong anticoagulation therapy, so the patients must be monitored periodically as they might develop haemorrhagic or thromboembolic complications. On the other hand, the biological prostheses do not present risk of thromboembolism, but their durability is limited, meaning that the timing of intervention is shortened. One of the possible solutions to the problems associated with the present biological and mechanical prostheses has been found to be polymeric heart valves. It has been shown, that they merge the superior durability of the mechanical valves with the enhanced haemodynamic function of bioprostheses.

Another significant drawback identified with regard to the heart valve prostheses is a limited availability of valves in different sizes, making most of them unsuitable in paediatric application. In addition, the fixed diameter of these valves causes them to have no growth potential proportional to the somatic enlargement of the patient. As a response to the problems associated with current valve prostheses for children and infants, it has been aim of the research to come up with the design of a pulmonary heart valve prototype which would be expandable in nature and comply with the established design criteria.

To allow the expansion of the prosthesis while its optimal functions are retained, the valve has been thought to be designed in a such fashion where the height of the prosthesis is adjusted for the application in adult, however to make the implantation possible in a child or infant, the radius of the base should fit the anatomy of a young patient. Such design would ensure that the annulus is adjusted to the anatomy of a child, whereas the leaflets initially oversized, would remain competent when the annulus is expanded with a child's somatic growth. Therefore, the leaflets would be able to fully close without a risk of leakage, and a valve made with suitable material could be expanded without needing to subject the patient to repeated surgical interventions. Nevertheless, deciding on the most optimal dimensions for this specific application can be quite challenging and might lead to incorrect assumptions, and in turn to misleading solutions. To obtain more reliable results, it was suggested that several models should be designed with three different sizes of annulus, and the effect of the valve height on the models should be investigated. Thus, the first step involved selection of three different sizes of the valves with three different Rb and Rc radiuses, so the models could be divided into three groups: small, medium and large. While the radii of base and radii of commissures were established, three different heights for the valves were suggested. The final result of the design process was obtaining nine different heart valve models in order to decide the optimal dimensions for the potential expandable heart valve.

The performance of nine pulmonary heart valve models was investigated by carrying out the simulation of the Newtonian steady blood flow through the pulmonary valve and pulmonary conduit. For this purpose, Computational Fluid Dynamic model using the finite volume method was used which allowed prediction of the impact of the products (the heart valve prostheses) on the fluid (blood). During simulation, dynamic solutions on the pressure distribution, velocity and wall shear stress were obtained.

When analysing the results on the pressure distribution through the pulmonary conduit, it has been observed that for all heart valve models, the value of the pres-

sure is declining towards the commissures of the valve, and has the lowest value at the outlet. It has been noted that although none of the models present considerable drops in the pressure, it is the most uniformly distributed in the case

of the large valves with Rb and Rc equal to 11 mm and 9 mm respectively, and also in the case of all three models with a height, H of 19 mm.

When considering the velocity of the blood flow through each of the models, it can be noticed that for all valves, the velocity increases after fluid passes from the area of a larger diameter to the area of the commissures with a smaller diameter, and then blood flow continues with the same speed towards the outlet. It means that the blood flow through the proposed models present typical behaviour for the pulmonary conduit, but with some differences in the speed of blood flow.

The last parameter obtained in the simulation was the wall shear stress which can be defined as the shear stress in the layer of fluid next to the wall of a pipe. In general, the magnitude of wall shear stress depends on how fast the fluid velocity increases when moving from the vessel wall toward the centre of the vessel. It has been observed that wall shear stress distribution in all the models is very uniform, with some exceptions at the point of contact between the leaflets and the conduit near to the inlet, as well between the entities where two leaflets intersect. All valve models present almost identical pattern for wall shear stress where in most cases the value is around 0 Pa, and only at some points it increases up to 25-27 Pa. Where the leaflets are attached to the inlet of the conduit the wall shear stress increases considerably and reaches the magnitude of 60 – 65 Pa.

The results of the simulation have been summed up in table 6, and the detailed description is presented below.

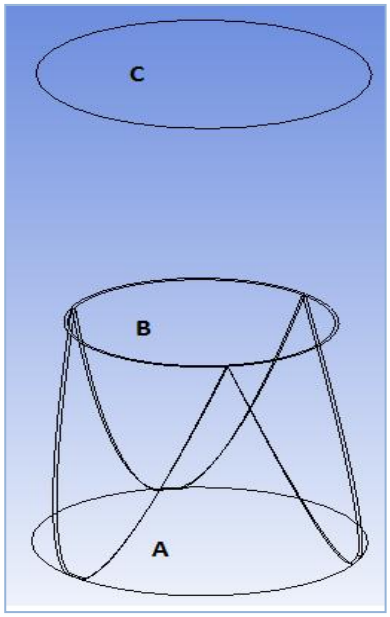


Figure 52. Schematic presentation of the pulmonary conduit and a valve. The area distinguished in the diagram are as follows: A – inlet of the pipe of the radius equal to Rb, B - commissures of the valve, C – outlet of the pipe.

Table 6. Summary of the results obtained during CFD simulation: pressure distribution (inlet and outlet), velocity and maximum wall shear stress.

Valve	Pressure [mmHg]	Velocity [m/s]	Max. Wall Shear Stress [Pa]
SV1	Inlet: 16.7 Outlet: 15.00	Inlet: 1.00 Outlet: 1.3	43
SV2	Inlet: 16.8 Outlet: 14.8	Inlet: 1.05 Outlet: 1.3	43
SV3	Inlet: 16.1 Outlet: 14.8	Inlet: 0.65 Outlet: 0.98	26
MV1	Inlet: 16.3 Outlet: 14.8	Inlet: 1 Outlet: 1.2	58 - 68
MV2	Inlet: 16.5 Outlet: 14.8	Inlet: 1 Outlet: 1.2	58 - 68

MV3	Inlet: 16.00 Outlet: 14.8	Inlet: 0.6 Outlet: 0.9	52 - 60
LV1	Inlet: 16.9 Outlet: 14.8	Inlet: 0.95 Outlet: 1.2	58 - 68
LV2	Inlet: 16.4 Outlet: 14.8	Inlet: 0.9 Outlet: 1.2	52-85
LV3	Inlet: 16.2 Outlet: 14.8	Inlet: 1.0 Outlet: 1.2	58 - 68

The results of the pressure across the plane passing through the pipe showed that pressure is most uniformly distributed for the valves with a height of 19 mm. It means that for these valve designs the pressure difference between the inlet and outlet is lower than for other models. According to the literature, pressure drop occurs when frictional forces, caused by the resistance to flow, act on a fluid as it flows through the tube - in this case the pulmonary conduit. The pressure drop has been found to be smaller for the models with H = 19 mm, so it can be assumed that a tall valve is also characterised by a lower resistance to forward flow. The lowest pressure drop has been found for MV3, meaning that this model presents the most uniform pressure distribution, and the lowest resistance to flow. It has been observed that for all models the highest value of pressure was found at the base of the leaflets where they are in contact with the pipe, and it reached approximately 17 mmHg. The main difference between the models is the surface area of regions of high pressure distribution which is largest for SV1 and SV2, and lowest for MV3. It can be assumed that the areas of the higher pressure are also the areas of the accumulation of the stresses, and therefore can be subjected to accelerated degeneration.

High shear stresses are the main problems in mechanical heart valve prostheses as they might enhance thrombus formation. As an important parameter in the evaluation of heart valve design, the wall shear stress at the wall surface of the pipe was identified. The results showed that for all models the wall shear stresses were very similar and presented only some variations. All designs were characterised by relatively low wall shear stress, with some increasing values in the distal part of the leaflets and between the entities of the upper edges of the cusps. The wall shear stress in this area rises up to approximately 65 -70 Pa for medium and large valves, and might be the cause of increased risk for thrombus formation in these areas. For SV1 and SV2 the wall shear stress was found to be lower than for medium and large valve with the value of approximately 43 Pa, whereas SV3 presents the lowest wall shear stress of around 26 Pa.

The velocity results indicated that the speed of blood flow increases while passing the area with radius Rc, and continues with the increased values towards the outlet of the pipe. For all valves, the blood flow can be assumed to be unidirectional. Three models with the height H = 19 mm presented results most resembling the normal velocity of blood in the pulmonary artery. MV3 has been found to be characterised by the values typical for the normal average blood velocity in the pulmonary artery, as the velocity for this valve ranges from 0.6 to 0.9 m/s.

Based on the results of the pressure distribution, velocity and the wall shear stress it can be concluded that the most optimal model has occurred to be medium valve 3 with Rb = 9 mm, Rc = 7 mm, and H = 19 mm. This model is characterised by the lowest pressure drop, and therefore the minimal resistance to forward flow which is one of the main haemodynamic requirements for an ideal heart valve. Moreover, it has been found that the velocity pattern of blood flow through MV3 present the most similar values to the normal velocity of blood flow through the pulmonary artery. The importance of this behaviour can be explained by the fact that too low velocity might be the reason for an increased risk of thrombus formation as the blood elements would attach to the walls of the leaflets and pulmonary conduit

forming the clot, whereas the high-velocity and multidirectional flow might lead to regurgitant and obstructive heart valve (Bulwer et al, 2011). Finally, the wall shear stress distribution showed that all valves are characterised by low stresses, however there are some points like the distal edges of the leaflets, and the area between entities of two adjacent cusps where the stresses are much higher and therefore they can be harmful for the arterial wall and leaflets, and accelerate thrombus formation.

5.1 Material recommendation – shape memory polymers

The choice of the material plays a very significant role in the application of the expandable heart valve prosthesis for the paediatric deployment. As mentioned in the previous chapters, the current objective of scientists is to obtain a valve which would grow with a child, so the repeated surgical interventions would be not needed. Although the aim is clearly specified, there are several limitations that prevent the scientists from accomplishing this goal, and therefore there are not too many scientific papers proposing a new solution.

After revising the limitations of the current prostheses in terms of products used for the fabrication of the valve, the research on innovative materials suitable for this application has been carried out. Finally, it was established to review the properties and possibilities offered by shape memory polymers as a possible alternative to present materials used for this purpose.

Shape memory polymers can be defined as materials which are able to change their shape in a controlled manner when applying an external stimulus such as temperature, light, electric or magnetic field. The shape-memory effect is not an intrinsic property - polymers do not display this effect by themselves. It results from a combination of polymer morphology and specific processing therefore it can be understood as a polymer functionalization (Peponi, 2014). By conventional processing (for example extruding or injection moulding), the polymer is formed into its initial, permanent shape B. Then, the polymer is deformed and fixed into the temporary

shape A during a process called programming. When applying an external stimulus, the polymer recovers its initial permanent shape B. This cycle of programming and recovery can be repeated several times, with different temporary shapes in subsequent cycles. In comparison with metallic shape-memory alloys, this process can take place in a much shorter time interval and polymers allow a much higher deformation rate between shapes A and B (Behl, 2007).

The first shape memory effect in polymers was reported in the 1960s by team of Rainer and his colleagues. This polymer consisted of a matrix of polyethylene irradiated with gamma radiation and as a result a material able to memorise its initial shape was obtained. From this moment, research on SMPs has become more popular due to their potential application in such areas as the biomedical sector, aerospace or textile industries. The growing interest in SMPs could be explained by their easy processability, low cost, softness and their versatility for easy design in specific applications by different techniques such as blending, making copolymers or adding fillers. Moreover, SPMs allow large, recoverable strains up to 400%. The strain is recovered through the action of an external stimulus, retrieving its initial shape. The possibility of using large strains gives more flexibility for fixing the temporary shape in contrast with metallic alloys and ceramics (table 6). With regard to their drawbacks, polymers present the worst mechanical properties and they do not tolerate great stresses. However, in order to overcome these drawbacks researchers have focused their interests in polymer composites based on the addition of fibres, fillers and nano-fillers to the polymeric matrix so improved properties such as stiffness or yield strength can be obtained (Peponi, 2014).

Table 7. Comparison of main properties in shape memory materials: metal alloys (SMAs), ceramics (SMCs) and polymers (SMPs) (Peponi, 2014).

	SMAs	SMCs	SMPs
Density [g/cm^3]	6 - 8	2	0.9 – 1.1
Recoverable strain	< 10%	1-4%	>400%

[%]			
Transition temperature [°C]	5 - 30	300	10 - 50
Biocompatibility and biodegradability	Biocompatible but cannot be biodegradable	Biocompatible but cannot be biodegradable	Biocompatible and can be biodegradable
Processing conditions	High temp. (>1000°c), high pressures	High temperature	Lower temp. (<200°C), low pressure
Cost [€/kg]	300	>500	15

Because of the possibility of SPMs to expand, and also several advantageous characteristics which place them over the shape memory alloys or ceramics, SPMs can be identified as a potential material for future application in heart valve prostheses. For instance, SPMs applied as the material of choice in the heart valve stent would enable expansion of the valve annulus without necessarily subjecting the patient to surgical interventions. By applying the appropriate external stimulus, a stent manufactured from SPMs would expand when it is needed, and allow the heart valve to adjust to the size of the native pulmonary conduit.

Shape memory effect has been reported in different types of polymers like thermosets, thermoplastics, elastomers, hydrogels and liquid crystals (Peponi, 2014). With several polymeric materials presenting potential for shape-memory effect, it seems possible to decide on the most suitable one which would comply with the design criteria for the paediatric deployment of heart valve prosthesis. Due to advanced technology, there are also many possible ways to improve some properties of these materials such as mechanical resistance, so they would become even more desirable (Peponi, 2014). Nevertheless, one of the limitations can be the external stimu-

lus used for the expansion of the material as they might be found hazardous when applied to the human body. Before deciding on the most suitable material, the type of stimuli programming needs to be reviewed. It has to be taken into account that some of them might cause adverse effects on the patient , for instance activation by the temperature exceeding the temperature of the human body could lead to enzymatic deactivation, disability or even death. In addition, possible stimulus also present in our everyday lives such as magnetic fields which might cause a sudden expansion when it is not desirable.

It has been shown in the previous chapters that polymers in general present advantageous properties over the metals and their alloys, as they are characterised by improved haemodynamic performance and durability. Therefore, there is large potential in using them in biomedical applications, and they may be perceived as a possible future solution to the limitations presented by the current prosthetic options.

5.2 Model limitations

While analysing the results of the simulation and considering the most optimal solutions, it has to be taken into account that the described CFD modelling presents some important limitations. First of all, the blood flow was assumed to be ideal steady Newtonian fluid with a constant viscosity and density. In reality however, blood is a non – Newtonian fluid where the viscosity depends on shear rate. Although, the assumption of Newtonian behaviour of blood is generally acceptable for large arteries because of high shear rate flow, it needs to be noticed that some significant differences might be found between these two approaches. Moreover, for the simulation of the blood flow, models of the valve leaflets without the stent design were used. It has to be verified that simulation of the blood flow through a leaflet – stent design would present different pressure, velocity and wall shear distributions and could affect the final decision on the optimal model. In addition, it has to be noted that simulation was carried out for a static valve in the fully open position only, whereas it would be recommended to conduct simulation through the full cycle of the heart in order to obtain full information on the performance of the

valve. Finally, the last limiting aspect of the research can be the thickness of the leaflets which was based on the suggested cusps thickness values for the polymeric heart valves, instead of identifying the most optimal value through analysis of their durability.

6. Conclusions and recommendations

Heart valve replacement in children remains a complex and challenging procedure due to several clinical and technical problems. In the review of currently available prosthetic options for paediatric deployment, several limitations were acknowledged. The mechanical valves were found to be durable, providing longer endurance of the prosthesis, and more importantly they are available in different ranges with some small sizes (16-18 mm) suitable for younger patients. Nevertheless, they are still not applicable in infants and very young children who require prostheses with even smaller annulus diameters. It has been found that the haemodynamic profile varies with size and very small prostheses have inferior flow properties. Another major drawback of the mechanical prostheses is a need for life-long anticoagulation therapy to prevent thromboembolism. Anticoagulation in children in some cases might be even more challenging than in adults due to a lack of compliance with the medication and activity restraints. Theoretically, this might lead to a higher risk of haemorrhage in children. When considering the biological prostheses, it was recognised that although they present great haemocompatibility, thus eliminating the risk of thrombogenicity, their main limitation is failure by degeneration, which gives them a shorter durability. A possible solution to these conventional prostheses is introduction of polymeric heart valves. It was found that they might be an optimal alternative as they join the advantages of the current mechanical and biological valves – they merge an improved durability with an enhanced haemodynamic function. Moreover, polymeric valves would offer an ideal solution for the most significant trends in the area of heart valve replacement, represented by minimally invasive approaches where the prosthesis can be collapsed into small catheters and delivered through the endovascular system. The use of polymeric leaflets could overcome the limitations of the xenograft tissues such as pericardium; enabling a reduced collapsed diameter, easier storage, application of consistent manufacturing techniques and avoiding the dehydration of the tissue that occurs during crimping.

Although the polymeric heart valves seem to be an ideal solution, they still present the main limitation with regard to prostheses for children and infants. This problem is associated with the somatic outgrowth present with all available prosthetic options in paediatric deployment. The lack of optimal alternative leaves all young patients with the necessity to undergo repeated surgical interventions until they reach adulthood. One of the attempts to overcome the problems associated with commonly used prosthetic valves in children was found to be a modified version of the Melody valve. Two paediatric cardiac surgeons at Boston's Children Hospital in the USA came up with a new solution by developing a replacement mitral valve that can expand as a child grows. For this purpose they used a Melody valve by trimming the length of the prosthesis and crimping it down to its smallest size, so they were able to implant it into five children ranging from two months to six months old. Although Emani and his colleagues reported successful results of their innovative idea, some further researches revealed its limitations. It has been reported by Qunionez et al (2013) that although the Melody valve has demonstrated acceptable short-term function, the implantation techniques used to prevent left ventricular outflow tract obstruction and paravalvular leaks should be considered. In this way they indicated that the Melody valve used for the paediatric application is not free from drawbacks, and therefore its safety in the long term performance is questionable.

Until today, scientists and surgeons have not suggested any optimal solution which would satisfy the design criteria for paediatric heart valve prostheses, and thus would provide comfort and satisfaction of young patients and their parents. Considering the requirements and expectations towards the heart valve prostheses for children, the objective of the research was a proposal of new solution involving the expandable concept. It has been suggested that to obtain a valve with growth potential, the model must be designed in such a fashion where the size of annulus is adjusted for the application in a child, and where the height of the valve, and in turn size of the leaflets is adjusted for remaining competent when changing the position due to expansion. It means that while increasing the radius of base by expansion,

leaflets due to its optimal height of the valve would be able to stay in a position which prevents paravalvular leakage.

In order to test the performance of the proposed solution, and to identify if the proposed assumptions are correct, nine different models of the pulmonary heart valve were designed. These models were divided into three categories: small, medium and large, with each group having the same radius of base Rb and radius of commissures Rc. Then, for each group, three different valve heights H were also proposed.

To validate one of the proposed design strategies, the behaviour of each valve was simulated during steady Newtonian blood flow, using the finite volume method. The purpose of the simulation was to predict the impact of the blood flow on the heart valve models. The CFD modelling included the following steps: defining the geometry, mesh generation, defining the boundary conditions (specifying the behaviour of blood flow and properties at the boundaries), carrying out the simulation, and visualisation of the resulting solutions. The results included pressure distribution, velocity of blood flow, and the arterial wall shear stress.

The results of the pressure distribution, velocity and the wall shear stress showed that the most optimal model has occurred to MV3 with Rb = 9 mm, Rc = 7 mm, and H = 19 mm. This model is characterised by the lowest pressure drop, and therefore the minimal resistance to forward flow which is one of the main haemodynamic requirements for an ideal heart valve. Additionally, it has been found that the velocity pattern of blood flow through MV3 present the most similar values to the normal velocity of blood flow through the pulmonary artery. The importance of

this behaviour can be explained by the fact that too low velocity might be the reason for an increased risk of thrombus formation as the blood elements would attach to the walls of the leaflets and pulmonary conduit forming the clot, whereas the high-velocity and multidirectional flow might lead to regurgitant and obstructive heart valve. Finally, the wall shear stress distribution for MV3 presents low stresses,

with small exceptions at the base of the leaflets. However, the value of wall shear stress does not exceed 60 Pa in the most vulnerable areas.

In terms of the material choice for the leaflets and stent design, the optimal materials were suggested. With regard to the cusps of the valve model, it was assumed according to the literature review, that polymeric materials present very good haemodynamic properties with improved durability. Therefore, it would be an ideal solution for the paediatric deployment as it would eliminate the need for risky anticoagulation therapy, and for repeated interventions owing to the better longevity.

Based on the limitations of the proposed experiment, and also because of the limited time which was given to carry out this research, some future recommendations have been proposed. It is suggested to identify the influence of the stent – valve model on the pressure, velocity and wall shear stress distributions to verify behaviour of the blood flow when a stent is introduced. With regard to simulation, it is also recommended to compare the difference between Newtonian and non-Newtonian model of blood flow in order to verify if significant changes occur. Another suggestion is further examination of the performance of the proposed optimal solution by manufacturing the valve model and testing its properties in vitro, for instance mechanical resistance to local stresses. Finally, it would be desirable to identify the potential properties of SMP stent as an expandable material in order to find its limitations, and to propose possible solutions.

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