UNIVERSITY OF STRATHCLYDE
DEPARTMENT OF BIOMEDICAL ENGINEERING

VAD for Pediatric Practice, Current Status and Future Prospective

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Declaration of Authenticity and Author's Rights:

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.

Signed:

Date:

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Table of Contents:

Abstract:

Heart failure (HF) is one of the major causes of death and disability in modern clinical practice. The causes of heart failure are many, and a number of technologies have been developed to address this issue by providing support to the failing heart, both as a permanent solution and as a bridge to recovery. These devices, known as Ventricular Assist Devices (VADs), have evolved over recent years as genuine solutions to this major clinical challenge. However, these technologies are largely designed to support failing hearts in the adult population, generally in the older element of the age spectrum. Little has been done in recent times with respect to the development of implantable solutions for heart failure or insufficiency in children. There are many reasons for this, but primarily the relatively small number of children requiring these procedures, the challenges associated with growth, and the lack of physical space for such implantable circulatory support technologies in children are key limitations for the development and deployment of these technologies.

The main purpose of this thesis is to investigate possible solutions for providing ventricular assistance for children. The most common causes and medical situations leading to VAD deployment will be reviewed and the various different types of VADs will be discussed in some detail.

In addition the challenges relating to the economic challenges that have to be overcome, relating to the market size and materials employed will be considered with a view to developing an economically

viable and technologically feasible solution to providing VAD support in children.

The methodology of this research is based on reviewing all papers and research in this field using all appropriate databases.

Key Words:

- Axial Rotary Pump.
- Cardiomyopathy.
- Centrifugal Pump.
- Congenital Heart Disease.
- Continuous Blood Flow.
- Extracorporeal Membrane Oxygenation.
- Heart Failure.
- Heart Transplantation.
- Mechanical Circulatory Support Devices.
- Pediatric Heart.
- Positive Displacement Pump.
- Pulsatile Blood Flow.
- Ventricular Assist Device.

List of Figures:

List of Tables:

List of Abbreviations:

- **ASD:** Atrial Septal Defect.
- **BiVAD:** Bi Ventricular Assist Device.
- **BPM:** Beat Per Minute.
- **BSA:** Body Surface Area.
- **BTD:** Bridge to Decision.
- **BTR:** Bridge to Recovery.
- **BTT:** Bridge to Transplantation.
- **CHD:** Congenital Heart Disease.
- **CPB:** Cardiopulmonary Bypass.
- **DC:** Direct Current.
- **DT:** Destination Therapy.
- **ECMO:** Extracorporeal Membrane Oxygenation.
- **FDA:** Food and Drug Administration.
- **HF:** Heart Failure.
- **HTx:** Heart Transplantation.
- **ICU:** Intensive Care Unit.
- **IDE:** Investigational Device Exemption.
- **IP:** Implantable Pneumatic.
- **IVAD:** Implantable Ventricular Assist Device.
- **IVC:** Inferior Vena Cava.
- **LD:** Lastissimus Dorsi.
- **LVAD:** Left Ventricular Assist Device.
- **MCAD:** Muscle Powered Cardiac Assist Device.
- **MCSD:** Mechanical Circulatory Support Device.

- **MEC:** Muscle Energy Converter.
- **MPC:** Methacryloyloxyethyl Phosphorylcholine.
- **NHLBI:** National Heart, Lung, and Blood Institute.
- **PumpKIN:** Pumps for Kids, Infants, and Neonates.
- **PVAD:** Pneumatic Ventricular Assist Device.
- **REMATCH:** Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive heart failure
- **RPM:** Rotation Per Minute.
- **RVAD:** Right Ventricular Assist Device.
- **RVD:** Right Ventricular Dysfunction.
- **SVC:** Superior Vena Cava.
- **TOF:** Tetralogy Of Fallot.
- **VAD:** Ventricular Assist Device.
- **VE:** Vented Electric.
- **VSD:** Ventricular Septal Defect.
- **XVE:** Extended Vented Electric.

Important Definitions:

- **Adolescents:** is the stage between puberty and adulthood.
- **Adult:** is a fully developed human and mature.
- **Cardiac Afterload:** is the tension or stress developed in the wall of the left ventricle during ejection.
- **Cardiac Preload:** is the end volumetric pressure that stretches the right and left ventricles of the heart to its greatest geometric dimensions.
- **Child:** is a human between the stage of birth and puberty.
- **Extracorporeal or Paracorporeal:** is a machine or an action that is based outside the patient's body.
- **Extraventricular:** situated outside the ventricle.
- **Infant:** is a human between the ages of 1 month to 12 months.
- **Intracorporeal:** is a machine or an action that is based inside the patient's body.
- **Intraventricular:** situated inside the ventricle.
- **Newborn or neonate:** is a human between the age of birth and 28 days.
- **Pediatrics:** is the branch of medicine that deals with the medical care of infants, children, and adolescents.

Chapter 1: Introduction

1.1 Layout of Thesis:

The dissertation consists of 6 chapters. In the first chapter, a brief introduction to the topic, background of the history of the Mechanical Circulatory Support Devices, list of the 3 main categories of MCSDs with a brief summary of each type. Different classifications of VADs, National Heart, Lung, and Blood Institute program for VAD developments and ends up with the Ideal VAD features. In the second chapter, the anatomy background of the normal human heart, the coronary circulation, blood circulatory system, and how the embryonic heart develops. Then the chapter covers the most familiar diseases affecting the pediatric heart, the congenital heart diseases, and the myocardial dysfunctions. A list of indications for mechanical support in children is also mentioned in this chapter. In chapter three, all extracorporeal ventricular assist devices are listed and discussed in detail. The fourth chapters, also talks about the intracorporeal ventricular assist device, all of them are discussed in details. In chapter five, more discussion and comparison are made between different types of MCSD. ECMO is compared to VAD, the three main generations of VADs are compared among each others, continuous blood flow and pulsatile blood flow VADs are also compared. Then this chapter covers the surgical complications associated with VAD implantation, and finishes with the limitation facing the available VADs. The sixth chapter talks about the future work in this field, the new upcoming devices and the new possible source of power needed to operate the VAD.

1.2 Introduction:

Heart transplantation is still the gold standard for patients suffering from end stage heart failure, with more than 9,000 infants born with congenital heart problems annually in USA; just 400 of them will have their chance to get a new heart (1). Because of the shortage in donors, Mechanical Circulatory Support Devices are used to support the patient's heart whilst a long term solution is considered. In the last two decades mechanical support devices have been the focus of considerable development activity, offering a wide range of solutions for patients with end stage heart failure as a bridge to decision (BTD), bridge to transplant (BTT), bridge to recovery (BTR), or finally as a destination therapy (DT) for the whole life (2).

Until recently the most common and reliable solution for this problem was using venoarterial Extracorporeal Membrane Oxygenation (ECMO). ECMO can offer full cardiac support that can be applied rapidly; on the other hand it can be applied only for short time, over a few days in most cases with a few weeks being the extreme range of deployment (1). Centrifugal pumps are also used as an extracorporeal circuit in infants and children supporting them from a few days to a few weeks. Under both treatment modalities patients are confined to the ICU setting (3).

More advanced mechanical support devices are the Ventricular Assist Devices (VAD), which can support the patient's heart longer than ECMO. VADs can be divided into several categories depending on the

flow, place of implantation and the supporting system that can offer to the heart (3).

1.3 History of Pediatric Mechanical Support Devices:

The first report of VAD use was in 1967 when Dr. Debakey used a left atrial- axillary artery ventricular assist device (LVBP) in a teenager heart to recover him from postcardiotomy failure after mitral valve replacement. This was the first successful use of MCSD and the patient recovered after 6 months (1).

The use of centrifugal pump systems started in the 1970s, supporting infants and children in their early age (<6 Kg). This type of treatment had excellent reports at that time, but also it has the same problems with ECMO such as non pulsatile blood flow and a short support time (1).

During the early 1990s VAD systems emerged in greater numbers and configurations. Extracorporeal systems have been used in intermediate size children and the results were generally encouraging. Some problems emerged with the use of VAD systems, including those associated with thrombogenicity. However, the development of VAD's advanced and has been developed to be used in infants and small children offering both pulsatile and continuous blood flow modalities. Despite the huge advancement achieved in this field, there remains a compromise between clinical need and safety in the use of VAD's in the paediatric domain with none yet meeting the ideal criteria.

1.4 Mechanical Circulatory Support Devices (MCSDs):

The main purpose of MCSD is to save the patient's life in emergency cases. They are primarily used to support the patient's heart for short periods of time, but later devices have been developed to help the patient for longer periods. MCSD can be divided into three main categories:

- Extracorporeal Membrane Oxygenation (ECMO).
- Centrifugal pumps.
- Ventricular Assist Devices (VADs).

1.4.1 ECMO:

ECMO is the first solution used to support children suffering from heart failure. Lack of alternatives and the long time experience in applying ECMO as a treatment for respiratory and heart failure, make ECMO the main approach at the present time. The first child to have ECMO support was a 9 years old boy in the late 1980s, reported by Dr. Denton Cooley. This boy was supported for 12 hours until a suitable donor was found. This case was the beginning of use MCSDs in pediatric patients and has opened all the options for researchers in this field (4).

The ECMO circuit as shown in **Figure -1-** below consists of the following components:

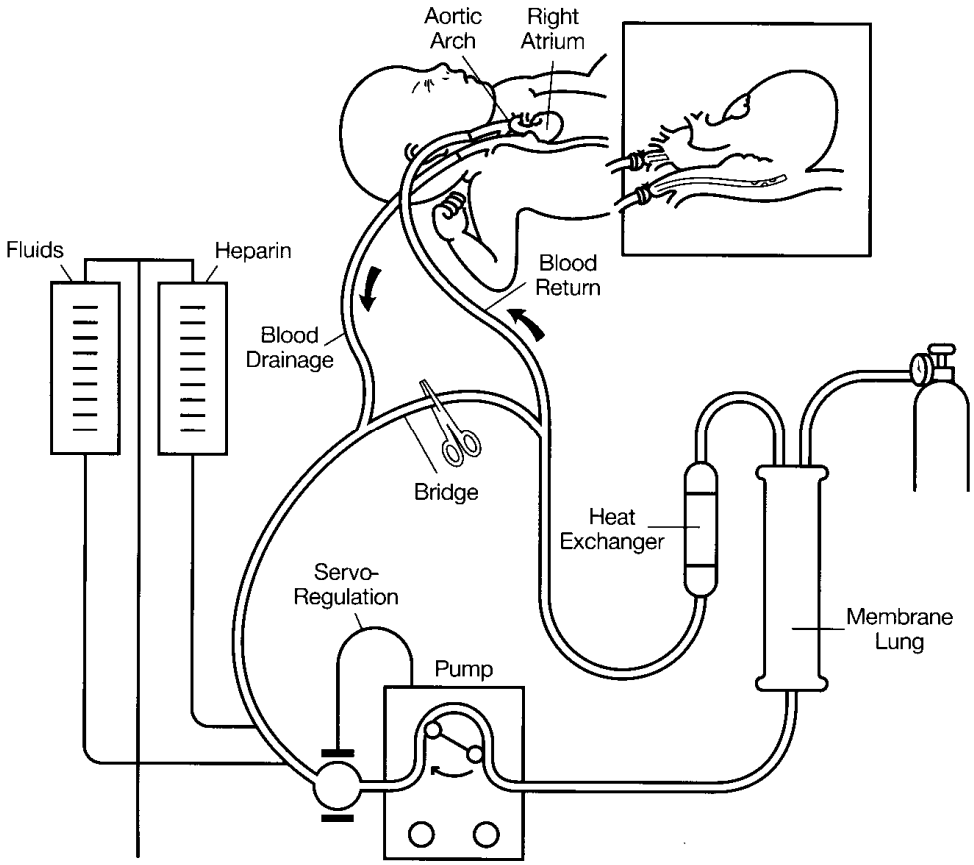

Figure 1 ECMO circuit (5)

- **Blood Pump:** Gravity drainage delivers blood from the patient's Right Atrium (RA) to a blood reservoir before the pump, the pump then pumps the blood from the reservoir to the other circuit components. It could be centrifugal pump or roller head pump.
- **Oxygenator:** or the artificial lung, where the blood status will be changed for deoxygenated blood into oxygenated blood. This oxygenator is connected to an external oxygen gas source to keep the gaseous exchange running.

- **Heat Exchanger:** is applied to keep the blood temperature at a fixed point.
- **Tubing Set:** a set of tubes and cannulae that used to connect the patient's heart with the other components. Special cannulae are used depending on the type of support applied on the patient. Some cannulae are directly applied on the heart while others are applied peripherally.
- **Monitoring System:** control and monitor all the components and the parameters like blood flow and temperature. Provide the user also with the appropriate alarms.

Due to the presence of the oxygenator it can also offer support for the lungs when the heart disease is associated with hypoxia, or pulmonary hypertension. In children the main causes of using ECMO are failure to recover from cardiopulmonary bypass (CPB) after cardiac surgery, or in the case of fulminant myocarditis (6) .

ECMO is associated with several complications due to the large artificial surface area of contact between the circuit and patient's blood which requires high level of anticoagulation. Some of these complications are thromboembolic, and bleeding. Using cannulae can also cause some problems such as infection due to the open chest, and immobilization. The continuous nonpulsatile flow could also be a possible cause of end-organ failure such as kidneys and liver, beside also the neurological complications. Short term support could be considered as one of the limitations in using ECMO, where it can be applied just for few weeks maximum (1). These problems caused ECMO

patients to have a high mortality with a 50% chance of survival and discharge from the hospital (7). On the other hand, ECMO still has some advantages such as supporting both heart and lung at the same time, biventricular support, quick and easy installation, accommodation of neonatal size limitations, inexpensive compared to the other solutions, and the large international neonatal and pediatric experience (5).

1.4.2 Centrifugal Pumps:

This system is very similar to ECMO but without the oxygenator and heat exchanger, it is also used for a short term support. The system consists of a centrifugal pump, control console, and a set of tubes that connects the patient's heart with the pump. A nonpulsatile flow is provided by a vortex technology, where an impeller rotates at a speed between 1,000 and 4,000 RPM to create a flow of 5 - 6 L/min (3), blood enters from the center of the pump and leaves from the side, blood path is shown in **Figure -2-**.

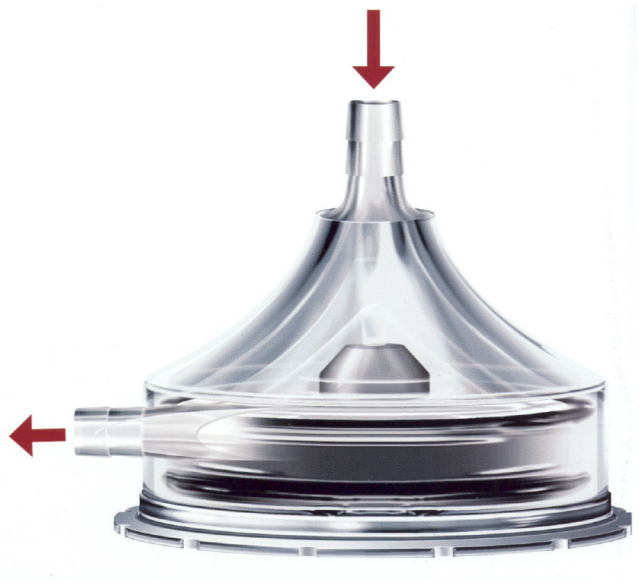

Figure 2 centrifugal pump (8)

The main advantage of this system is the low priming volume of the pump and short length of the tubing system, which allows its use in small patients <10kg (9). Several reports have described the successful use of centrifugal pumps in supporting a wide range of pediatric cardiac diseases (10). It is also a relatively inexpensive choice, and much easier for transporting the patient compared to ECMO (3). However the cannulation system is not very stable and this could be considered as a problem by not allowing the patient to move. Infection still exists in this system but to a lesser degree than ECMO. Anticoagulation substances are needed due to the contact between the blood and the artificial surface of the pump and tubes (5).

Figure 3 Bio Medicus Centrifugal Pump (8)

Several products have been used in practice such as Bio-Pump (Medtronic Bio-Medicus, Minneapolis, MN), as shown in **Figure -3-**, Capiox (Terumo, Ann Arbor, MI, USA) and Rotaflow (Maquet, Rastatt, Germany). Pump chamber is available with a variety of different sizes to

cover a wide spectrum of patients, very small priming volume pumps are specially produced for infants (11).

1.4.3 Ventricular Assist Devices (VADs):

The third option available for children with heart failure is using VAD. These devices have been in use since 1990s. VADs have several advantages over ECMO, such as pulsatile flow which leads to a better tissue perfusion, patients do not need to be totally paralyzed. In addition VADs can offer some degree of freedom for the patient where he/she can move and allow physical rehabilitation (12).

VADs can be divided into several categories depending on their outflow pattern, duration of support, the mechanism of the pump, and the connection between the device and the patient.

According to the **outflow pattern** VADs can be divided into pulsatile flow and continuous flow:

- **Pulsatile Flow:** the blood flows in series of pulses, like the blood flow produced by a normal heart. Those devices are very large and in most cases placed outside the patient's body.
- **Continuous Flow:** the blood flows continuously in this type of VAD by using axial flow pumps or centrifugal pumps. This type has several advantages like small size pump, no need for compliance chamber, no need for valves, low power consumption, and much more quiet than pulsatile flow pumps.

According to the **duration of support** VADs can be divided into short term support and long term support:

- **Short Term Support:** in this category the devices are used to support the heart for short time for a few days usually less than 30 days. They are applied until the decision is made, transplantation is ready, or heart is recovered. Mainly those devices are placed outside the patient's body.
- **Long Term Support:** these devices can be used for months or even years, mainly applied as a destination therapy and are totally implantable inside the patient's body.

According to the **mechanism of the pump** VADs can be divided into positive displacement pumps, axial flow pumps, and centrifugal pumps (13):

- **Positive Displacement Pumps:** they are also called the first generation VADs; these pumps have a pulsatile outflow. The pump is either driven pneumatically by compressed air, or electrically by an electric motor.
- **Axial Pumps:** also called the second generation VADs. These pumps have a continuous outflow.
- **Centrifugal Pumps:** the new generation of VADs is using magnetically levitated impellers with centrifugal pumps. This type is still under development.

According to the **support system applied on the heart** VADs can be divided into RVAD, LVAD, and BiVAD:

- **Right Ventricular Assist Device (RVAD):** support the right ventricle.

- **Left Ventricular Assist Device (LVAD):** support the left ventricle.
- **Bi Ventricular Assist Device (BiVAD):** support both left and right ventricles, it could be also called artificial heart.

According to the **connection between the device and the patient**, VADs can be divided into extracorporeal (paracorporeal) devices and intracorporeal devices:

- **Extracorporeal Devices:** those VADs are placed outside the patient's body, they need special care and the patient should stay in the ICU all the time. Mainly used as a short term support systems.
- **Intracorporeal Devices:** those VADs are totally implantable inside the patient's body, apart from the external power source and the controller. All that you have is just a percutaneous cable outside the patient for control and power.

The last classification is the most important one in many ways as it represents the ideal VAD solution, one which is in-dwelling and renders the patient independent of the ICU setting over prolonged periods of time.

1.5 NHLBI VAD Program:

Due to the lack of available VADs for pediatric patients and the perceived clinical need in this sector of activity, the National Heart, Lung, and Blood Institute (NHLBI) has granted a full funded program to develop a pediatric VAD. The first phase of this program was launched on March 2004 for five years duration, with funding totaling $22 million (12). The companies involved in the program are:

- **Pedia Flow** (University of Pittsburgh; Carnegie Mellon University; Children's hospital of Pittsburgh; Launch point, LLC; and World Heart)
- **PediPump** (The Children's Hospital at the Cleveland Clinic; The Department of Biomedical Engineering, The Cleveland Clinic Foundation; Foster-Miller Technologies, Inc.)
- **Pediatric Cardiac Assist System pCAS** (Ension Inc.; University of Louisville; Seare Biomatrix Systems; Fluent, Inc.)
- **Infant and Children-size Jarvik 2000** (Jarvik Heart Inc.; University of Maryland Medical Centre; Mississippi State University; Whalen Biomedical, Inc.)
- **Pediatric Ventricular Assist Device PVAD** (Pennsylvania State University; Minnetronix, Inc.)

The second phase of this program started in January 2010, and four companies were awarded a total of $23 million to start preclinical testing of implantable pediatric VADs. This new phase was called Pumps

for Kids, Infants, and Neonates (PumpKIN) (5). The companies involved in this phase are:

- **Pediatric Cardiac Assist System pCAS** (Ension Inc., Pittsburgh, PA)
- **Levitronix PediPL** (Levitronix LLC, Waltham, MA)
- **Pedia Flow** (PediaFlow VAD Consortium, Pittsburgh, PA)
- **Jarvik 2000** (Jarvik Heart Inc., New York, NY)

All these devices will be discussed in detail later in this thesis.

1.6 REMATCH Study:

The greatest benefit of using VAD therapy was demonstrated in the REMATCH study (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive heart failure) which took place from 1998 to 2001. All patients were suffering from heart failure and were not eligible for heart transplantation. Two randomized groups of patients received either conventional medical therapy or received LVAD (HeartMate XVE, II) both VADs are extracorporeal pulsatile blood flow pumps. After one year the LVAD group showed 52% survival rate compared to 23% in the medical therapy group. After two years the LVAD group showed 23% while the medical therapy one showed only 8% survival rate. On the other hand patients in the LVAD group were more likely to have adverse events like bleeding and infection, and there were some cases of mechanical device failure (19).

Although the REMATCH study was oriented towards adult patients, it showed the great effects of using a LVAD in supporting

patients with congestive heart failure. These positive indications bring to attention the possibility of success in pediatric patients also.

1.7 The Ideal VAD:

The main purpose of all research in VAD systems is to find a fully implantable device for small children. The ideal VAD should fulfill the following requirements:

- **Durable:** this VAD should stay for the whole life with the patient.
- **Reliable:** since the device is implanted inside the patient's chest, there should be no chance for any type mechanical failure.
- **Adequate Flow:** VAD should provide enough cardiac output to keep organs function perfectly.
- **Quiet:** VAD should be completely silent whilst running.
- **Small and lightweight:** since this VAD is designed for small children, size and weight are the major parameters which should be noticed carefully.
- **Modular System:** the system should be capable of providing cardiac support across a wide range of patient sizes, ranging from neonates to young adults.
- **Immunological Inert:** should not cause any type of immunological complications which may affect other organs.
- **Resistant to Infection:** should be totally sterilized.
- **Resistant to Thrombosis:** thrombus formation is very dangerous and could cause problems for other organs.
- **No Need for Anticoagulation:** no bleeding problems in future.

- **Fully Implantable:** no need for percutaneous power cable or vent line.
- **No External Power Source:** no need to carry sets of batteries all the time, the new power source could be inside the body.
- **Easy Operation:** easy in implantation, does not need complicated equipment in implanting or operating.
- **Cost Effective and Affordable:** all patients could afford it, by using cheap materials.
- **Forgettable:** patient should not notice that he/she is connected to a VAD.

Chapter 2: The Pediatric Heart

2.1 Anatomy of the Normal Heart:

2.1.1 The Heart:

The heart is the most important working muscular organ in all living animals, playing a major role in providing enough oxygenated blood with nutrients to all the living cells and collecting the metabolic waste products in its way back. The heart is located in the anterior chest wall directly posterior to the sternum, connected with the great blood vessels, the aorta, the vena cava, the pulmonary arteries, and pulmonary veins, which are connected to the heart's base as shown in **Figure -4-** and **-5-**. The base of the heart is located posterior to the sternum at the level of the third costal cartilage shifted 1.2 cm to the left side. The apex is the inferior end of the heart, located in the fifth intercostal space, and shifted 7.5 cm to the left of the midline. The normal adult heart measures 12.5 cm in length from the base to the apex, it has a mass between 250g and 350g and is about the size of a fist. The adult's heart usually beats between 60 and 100 times a minute, while the baby's heart may beat up to 190 times a minute. During an average lifetime, the human heart will beat more than three billion times, pumping more than 160 million liters of blood (14).

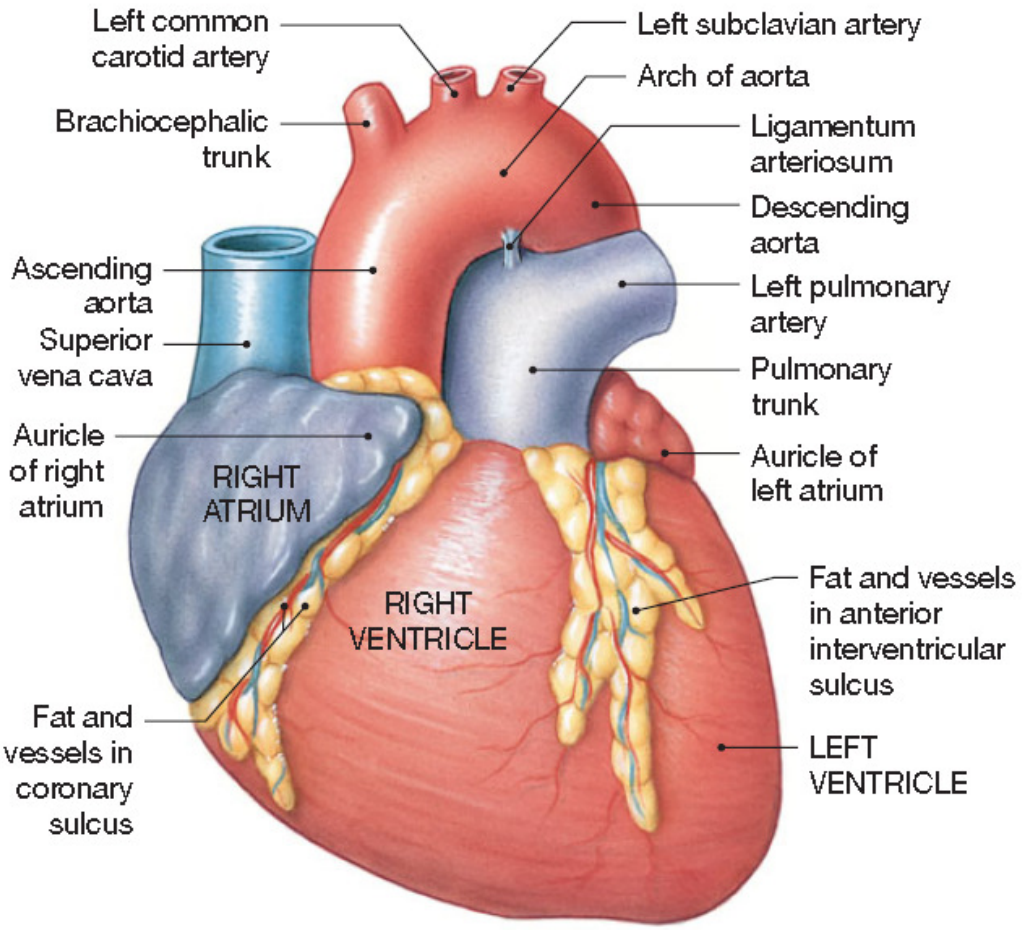

Figure 4 The Heart (14)

The heart wall consists of three main layers, the epicardium, the myocardium, and the endocardium. The first layer covering the outer surface of the heart is the epicardium; this layer consists of an exposed mesothelium and an underlying layer of loose areolar connective tissue which is connected with the second layer. The second layer is the myocardium, which is the main muscular layer forming the atria and ventricles. This layer consists of concentric layers of cardiac muscle tissue; it contains also blood vessels and nerves. The third layer is the endocardium which covers all the inner surfaces of the heart including

the valves. The thickness of the heart wall is not equal in all heart chambers, the left ventricle has a thicker wall which enables it to pump the large systemic circuit thorough the body at a high arterial pressure (14).

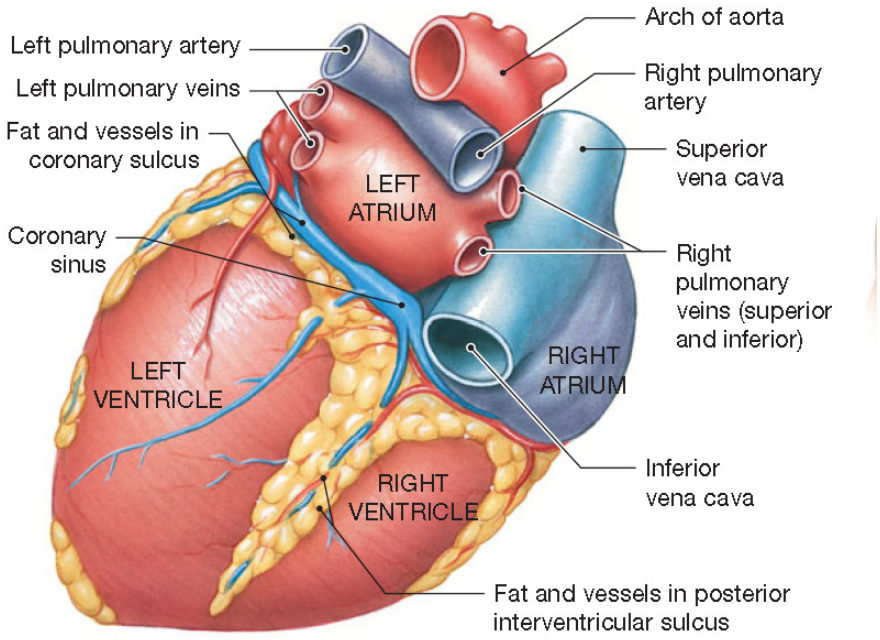

Figure 5 The Heart (14)

The heart consists of four main chambers; two ventricles and two atria, as shown in **Figure -6-**. The right atrium is located on the top right side of the heart, receives the deoxygenated blood from all parts of the body through the superior vena cava (SVC) and the inferior vena cava (IVC), and is connected with the right ventricle through the tricuspid valve. The left atrium is located on the top left side of the heart, receives all oxygenated blood from the left and right lungs through the pulmonary veins and delivers this blood to the left ventricle through the mitral valve. The right ventricle is located on the right bottom side of the heart, receives the deoxygenated blood from the right atrium and

pumps it to the left and right pulmonary arteries through the pulmonary valve to the left and right lungs. The left ventricle is located in the left bottom side of the heart, receives the oxygenated blood from the left atrium and pumps it to the whole body throughout the aortic valve and the aorta, the aorta is then divided into several branches to cover all parts of the human body. A thick muscular wall called the septum separates the right side and the left side of the heart. In each heart beat, the right side of the heart pumps the same amount of blood into the lungs, and the left side of the heart into the body. Commonly, physicians refer to the right atrium and right ventricle as the right heart, and the left atrium and the left ventricle as the left heart (14).

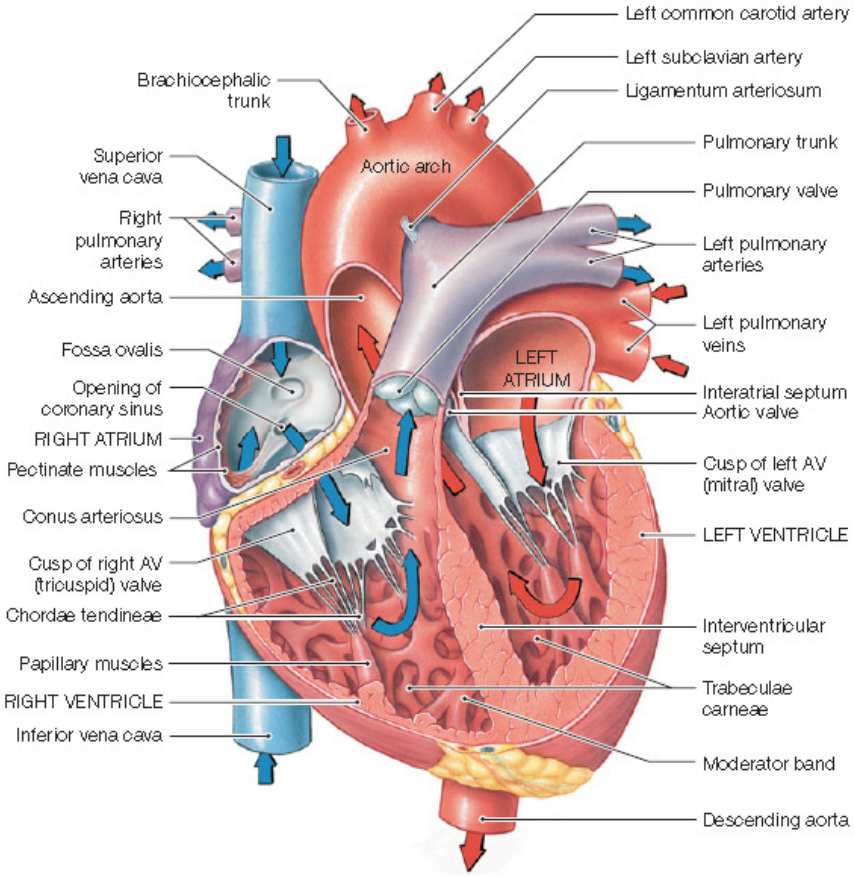

Figure 6 Heart Valves (14)

2.1.2 The Coronary Circulation:

Since the heart is a continuously working pump, it needs energy to keep on working all the time. This energy is provided by the coronary circulation, which supplies the heart and its muscular cells with the oxygen and nutrients needed and removes all the waste products. The coronary circulation, shown in **Figure -7-**, consists of the left and right coronary arteries which are branched from the ascending aorta, and the cardiac veins which are connected to the right atrium near the base of the inferior vena cava. The coronary circulation is very important, any blockage for this circulation, even partially blockage, will cause a reduction in the cardiac performance and can result in a heart attack. This blockage in the coronary circulation system is called Coronary Artery Disease (CAD) (14).

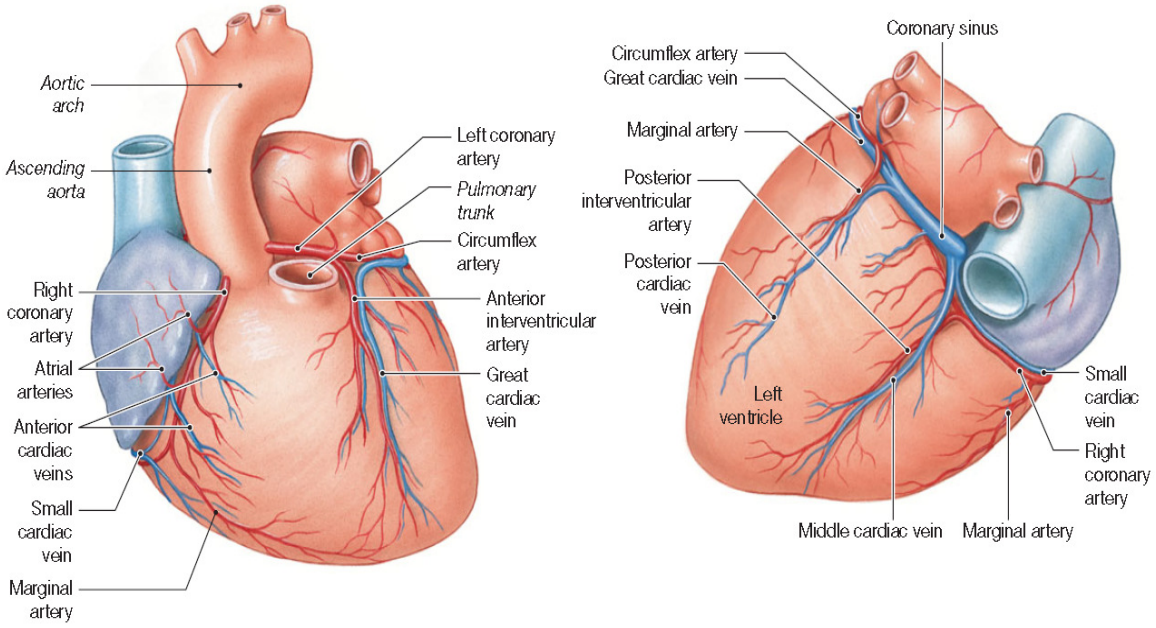

Figure 7 The Coronary Circulation (14)

2.1.3 The Blood Circulatory System:

The blood circulatory system, shown in **Figure -8-**, consists of the heart and two blood circuits connected with it; the pulmonary circuit, and the systemic circuit. In the pulmonary circuit, the deoxygenated blood from all parts of the body is collected in the right side of the heart, then pumped to the lungs, where the gaseous exchange occurs and deoxygenated blood is oxygenated, and then comes back to the left side of the heart. In the systemic circuit, the oxygenated blood is pumped from the left side of the heart to all parts of the body to supply the tissues with oxygen and nutrients needed for their functions, and to collect the metabolic waste products from all living cells, then this deoxygenated blood is returned to the right side of the heart to close the circuit (14).

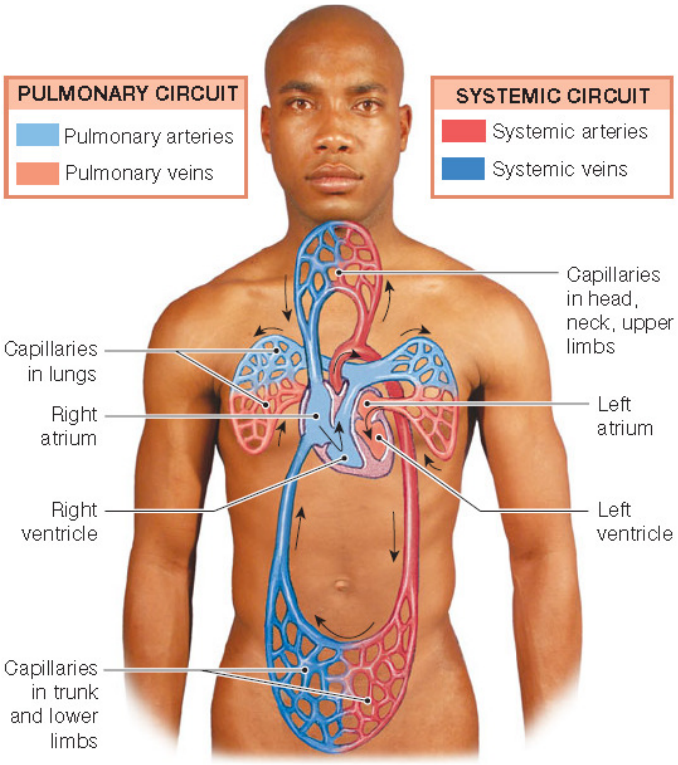

Figure 8 The Blood Circulatory System (14)

2.1.4 The Embryonic Heart:

There are several phases of fetal heart development. The first phase is the Tube Formation, between 15 and 20 days, where the heart has a shape of two bended tubes, and it started to beat at this stage. The second phase is the Looping, between 21 and 28 days, in this stage distinct chambers start to appear, the left and right ventricles became more obvious. The third phase is the Atrial Septation, between 34 and 50 days, where the septum grows from the ventral wall of the atrium and forms a ridge on the posterior wall of the atria. The fourth phase is the Outflow Tract Septation between 35 and 56 days, in this stage the outflow tract begins as single tube connected with the ventricles, by the end of this stage the aorta and the pulmonary outflow are separated and connected to the left and right ventricles respectively. The fifth phase is the Ventricular Septation, between 38 and 45 days, in this phase the separation between the ventricles is completed (15). Development of an embryonic heart is a very complicated process; any small change during this process can cause congenital heart disease of the fetus.

2.2 Congenital Heart Diseases:

Congenital Heart Disease (CHD) is any defect or change in the structure of the normal heart and the main vessels connected with it, which it appears directly after birth. The chance of having congenital heart disease is 6 in 1000 births, and occurs in similar frequencies in each part of the world with all ethnic groups of people (16) .

Congenital heart disease can be classified depending on the direction of blood flow through intracardiac shunts. Blood flowing from left side to the right side of the heart is called acyanotic defect. Arterial Septal Defect (ASD) is an example of the acyanotic defect, where the blood flows from the left atrium to the right atrium. The oxygenated blood in the left atrium is mixed with the deoxygenated blood in the right atrium, which causes an increased volume load on the right atrium. The other case when the blood is flowing from the right side to the left side of the heart is called cyanotic defect. The most common example is Tetralogy of Fallot (TOF), where the right ventricle outflow tract is narrowed. In TOF the deoxygenated blood in the right ventricle faces great resistance to flow into the pulmonary artery, and as a result blood then follows the lower resistance path which is the ventricular Septal Defect (VSD), and flows to the aorta without undergoing gaseous exchange in the lungs. Some children may suffer from both cases together; this case is called mixed lesion CHD or complex CHD (17).

Infants with complex CHD may suffer from poor nutrition due to their poor appetites, which can have a substantial effect on their normal growth. Unrepaired CHD in the early stages of life increases the risk of morbidity and mortality due to underlying cardiopulmonary compromises (17).

2.3 Indications for Mechanical Support in Children:

There are huge differences between pediatric heart failure and adult heart failure. Usually, pediatric patients with cardiac heart diseases have more complicated issues associated with their case, like right ventricular failure, or pulmonary hypertension. In this case, to overcome these challenges, pediatric patients require particular care for each individual patient from the care-providing team in the hospital. This team should involve the following specialties: cardiologist, cardiac surgeon, cardiac anesthesiologist, neonatologist, respiratory therapy, perfusion specialist, pharmacology, infection disease specialist, pulmonologist, nephrologists, haematologist, and a well trained nursing staff (18). Pediatric patients will require some kind of mechanical circulatory support in the following situations:

2.3.1 Myocardial Dysfunction:

Children suffering from myocardial dysfunction can be classified into two main groups; bridge to recovery in reversible dysfunction cases, and bridge to heart transplantation in more severe cases. Pediatric patients suffering from reversible myocardial dysfunction can be treated with MCSD as a bridge to recovery. Reversible myocardial dysfunction includes post cardiotomy myocardial dysfunction, acute myocarditis, or acute post transplant rejection. Children with end stage congenital heart disease, and prolonged graft rejection after heart transplantation, are candidates for long term support with MCSDs as bridge to transplantation or in other cases as a destination therapy (18).

2.3.2 Cardiopulmonary Resuscitation:

MCSDs are used to rescue the patient's heart after failure of conventional resuscitation. All cardiac intensive care units should be able to support the patient with MCSD, in this case, in a matter of a few minutes (18).

2.3.3 Preoperative Stabilization:

MCSDs are used to support pediatric patients with cardiovascular collapse, or severe hypoxemia before any surgical intervention is undertaken. Some cases that are considered under this situation are pulmonary hypertensive crises, total anomalous pulmonary venous connection, tetralogy of Fallot with absence of pulmonary valve, or Ebstein's anomaly (18).

2.3.4 Acute Respiratory Distress Syndrome:

ECMO is the main option for parenchymal lung disease in pediatrics. Patients with congenital heart disease are more prone to develop parenchymal lung disease before or after their cardiac surgery. ECMO is used for a few weeks to support patients suffering from parenchymal lung disease, allowing more time for the lungs to recover (18).

2.3.5 Malignant Dysrhythmias:

In some rare cases, patients who fail conventional aggressive medical therapy for continuous tachydysrhythmias may be suitable for short term support with MCSDs. Patients in this case may suffer from lethal arrhythmias associated with myocardial disease, supraventricular tachycardia, ventricular tachycardia, or junctional ectopic tachycardia (18).

2.3.6 Profound Cyanosis:

Pediatric patients diagnosed with cyanosis need to be corrected. MCSDs can be used to support these patients on a case by case basis. Some other alternative options could be possible to help patients with cyanosis, but MCSDs are used if all the previous options fail (18).

2.3.7 Dilated Cardiomyopathy:

Cardiomyopathy disease is a disease that affects the heart's muscle or in other words the heart's wall. Cardiomyopathy includes abnormal changes in the size of the heart chambers, the wall thickness, or abnormalities in heart functions such as systolic or diastolic dysfunctions. Dilated cardiomyopathy is the most common type of cardiomyopathy in the world; in this case the left ventricle or the ventricles are dilated and contract very weakly (19).

Chapter 3: Paracorporeal Ventricular Assist Devices

VADs which are located outside the patient's body are called paracorporeal or extracorporeal VADs. These devices can suit a wide range of patient sizes from neonates to adults, offer both types of blood flow (continuous and pulsatile), they can be used for short or medium term as a BTR, BTD, or BTT. The main paracorporeal VADs are:

3.1 Thoratec Paracorporeal VAD (PVAD):

This VAD was first developed by Penn State University in the 1970s. Thoratec PVAD, as shown in **Figure -9-**, is a pneumatically driven pulsatile flow pump, and was designed for short to medium term support, offering left, right, or biventricular support. In 1995 it was FDA approved as a BTT and in 1998 also was FDA approved as a BTR (2). Thoratec PVAD consists of a rigid chamber made of plastic and consists of two separate chambers; one for blood and the other for the driving air. The chambers are separated by a multilayer flexible polyurethane sac. Air is provided from an external compressor that pushes the sac and forces the blood to eject, which can offer 65 ml stroke volume, which equals blood flow up to 6.5 L/min at a maximum rate 100 BPM. Two mechanical valves (Bjork – Shilly concave convex tilting disk) are placed in the blood inflow and outflow path to ensure unidirectional flow. The inlet cannula is connected to the left atrial or left ventricular apex, and the outlet is connected to the aorta. The control console can offers three modes of driving the pump: asynchronous (fixed rate), synchronous (timed to the patient's heart rate), and volume mode.

PVAD is 125mm x 80mm x 60mm and weighs 417g, and can be used for both pediatric and adult patients, since the device is placed outside the body. It has been used to support patients less than 17kg successfully, the longest duration of using this VAD was 1204 days (20).

Figure 9 Thoratec PVAD (5)

Thrombosis and infection are the main problems associated with this device due to the ports of the cannulae and the contact between the blood and the large artificial surface (20). Large stroke volume pumped into a small aorta is also considered as one of the problems, which limits the use of this VAD in small children (12).

3.2 Berlin Heart EXCOR:

The Berlin Heart EXCOR, as shown in **Figure -10-**, is a paracorporeal pulsatile VAD, driven pneumatically by compressed air. It was first developed in 1989 for adults at the German Heart Center in Berlin, and the pediatric version has been available since 1992 (5). This VAD has a translucent polyurethane housing, which consists of two chambers, one for blood and the other for compressed air, with a multilayer flexible membrane used to keep the chambers separated. Silicone cannulae are used to connect the pump with the patient's heart, and polyurethane valves are placed inside the pump to maintain unidirectional flow. The maximum flow rate which can be delivered is 10 L/min at 150 BPM pump rate (2). Berlin Heart EXCOR is combined with the driving unit IKUS 2000, which offers both mono and biventricular, support with several modes synchronous, and asynchronous (3).

Berlin Heart EXCOR has several advantages such as the variety of pump stoke volumes 10,25,30,50,60, and 80 ml, which makes this device the best solution for pediatric and neonate patients, **Figure-11-**. The translucent chamber allows thrombus formation to be visualized and prevent more complicated conditions. This device is placed outside the patient's body which allows easy changing of the pump if there is any problem with it (11).

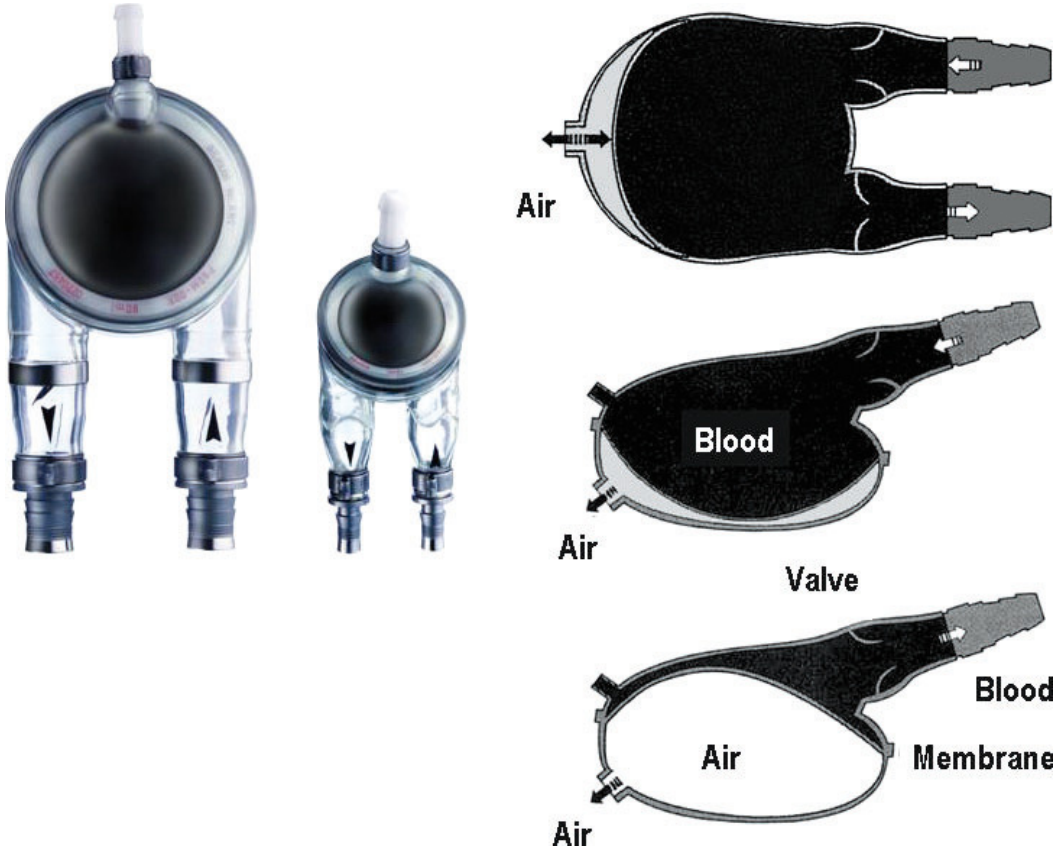

Figure 10 Berlin Heart EXCOR (3)

Hetzer et al., (2006) has reported his experience with Berlin EXCOR for 15 years, supporting 68 children mean age 7.6 years (2-17 years). The mean support time was 35 days (0- 420 days); the survival rate until transplantation or after weaning was 62% (21).

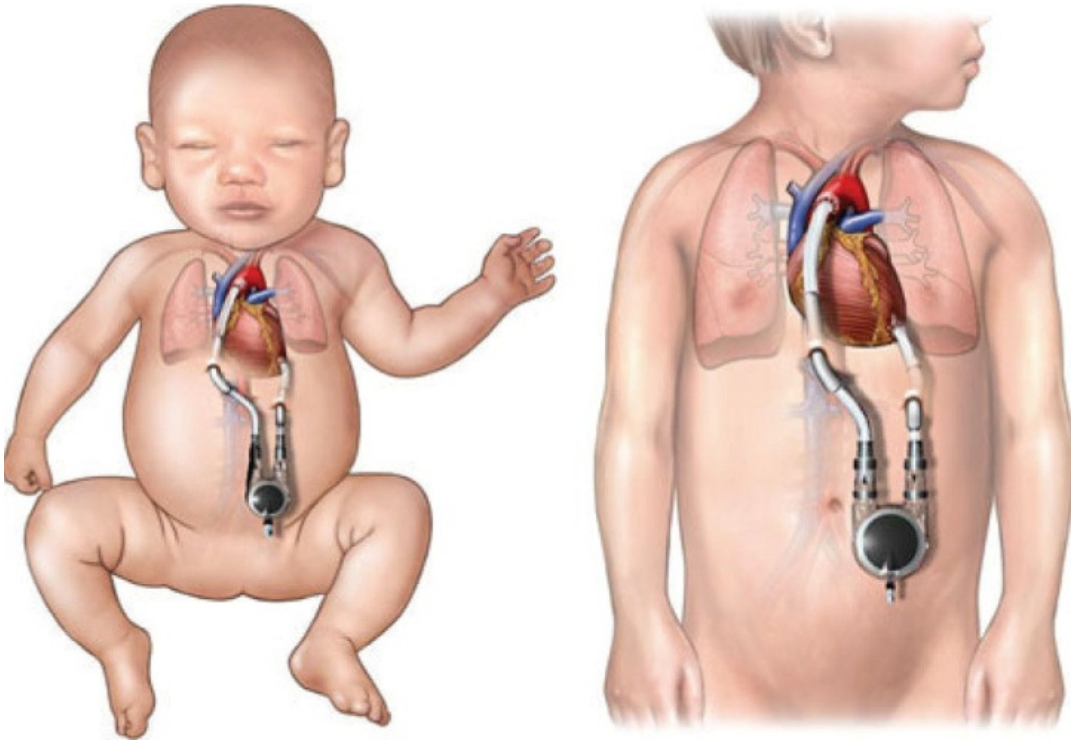

Figure 11 Berlin Heart EXCOR (22)

This device has been used in more than 30 medical centers in the USA with survival rate up to 75%, and more than 2000 devices have been implanted worldwide. CE mark was received in 2000; FDA approval was gained in 2011 as an Unconditional Investigational Device Exemption (IDE) (2). On the other hand, it still has major problems such as restriction on mobility, infection, and thrombosis (12).

3.3 MEDOS HIA VAD:

MEDOS **(Figure -12-)** is a paracorporeal pulsatile pump pneumatically driven, it was first developed in Aachen, Germany in 1994 (5). The design is very similar to Berlin Heart EXCOR, it has a translucent housing made of polyurethane, available in different left ventricular sizes (10, 25, 60 ml stroke volume), and different right ventricular sizes (9, 22.5, 54 ml stroke volume), with two chambers separated by a multilayer membrane. Tri-leaflet polyurethane valves are also used to keep the flow in one direction, compressed air is provided from an external unit. MEDOS can be applied as LVAD, RVAD, or BiVAD (1). Although several studies have reported using MEDOS successfully, the Berlin Heart EXCOR is still preferred in medical centers (23).

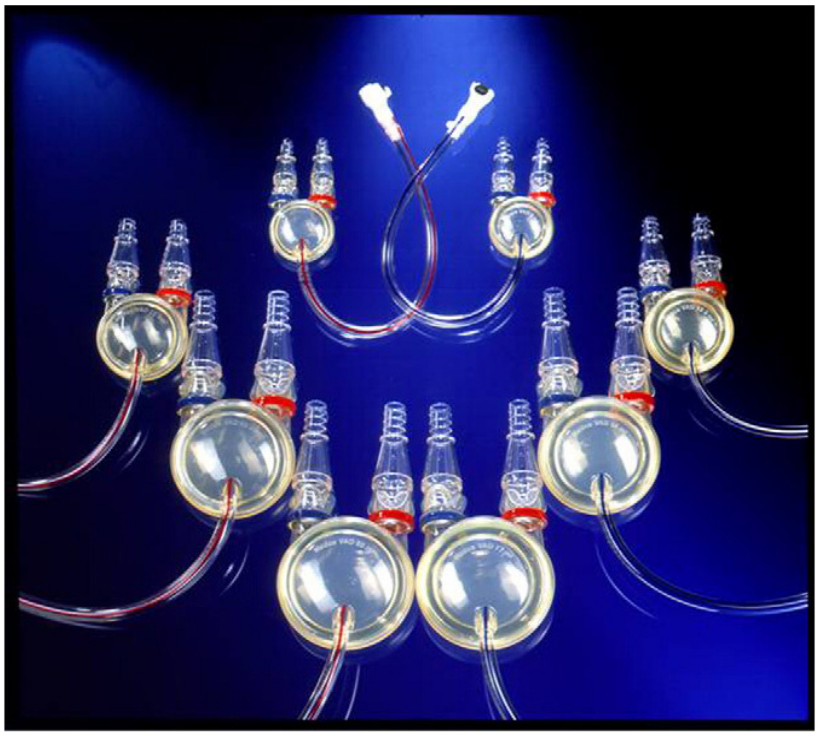

Figure 12 MEDOS VAD (5)

3.4 Abiomed Biventricular Support 5000:

Abiomed BVS 5000 is a pneumatically driven pulsatile VAD, and is one of the earliest models approved by FDA for BTR. It is used for short term support (7 to 10 days) and requires the chest to be left open (24). This pump can support one ventricle or both ventricles, with a maximum flow rate of 6 L/min. The pump housing is made from clear plastic and connected to the heart through silicon tubes, two valves are placed inside the pump to keep the flow in one direction (20). It depends on an air compressor to drive the pump. Although it is suitable for patients with BSA >1.2 m^2, it has been reported supporting a 14 year old boy for 3 days (25).

3.5 Abiomed AB 5000:

Abiomed AB5000 is a paracorporeal pneumatic VAD, which received FDA approval for BTR in 2003. AB 5000 is an ambulatory version of Abiomed BVS 5000, allowing more mobility for the patient. It has a similar design to the previous model; the translucent chamber contains a flexible membrane, and 2 tri- leaflet valves. It is lighter than BVS 5000, weighs 230 g, and is used to support patients for a longer duration than BVS 5000; the longest duration recorded was 57 days (2).

3.6 Penn State PVAD:

Pennsylvania State University is developing a pediatric VAD under the NHLBI first phase program, based on the design of adult size Pierce-Donachy VA. Penn State PVAD is a pneumatic VAD, offers a pulsatile blood flow, used for medium duration up to 6 months, it can be used in both implantable or paracorporeal mode (12). This system, shown in

Figure -13-, offers support for both ventricles, and it is available in two sizes. The small version is for infants ranging from 5 to 15 kg, flow rate ranging from 0.5 to 1.3 L/min, and 12 ml stroke volume. The large version is for children ranging from 15-35 kg, flow rate ranging from 1.3 to 3.3 L/min, and 25 ml stroke volume (11). Recently a study reported testing Penn State VAD in an animal model. 16 sheep were supported for 4 weeks, and the results were generally positive (26).

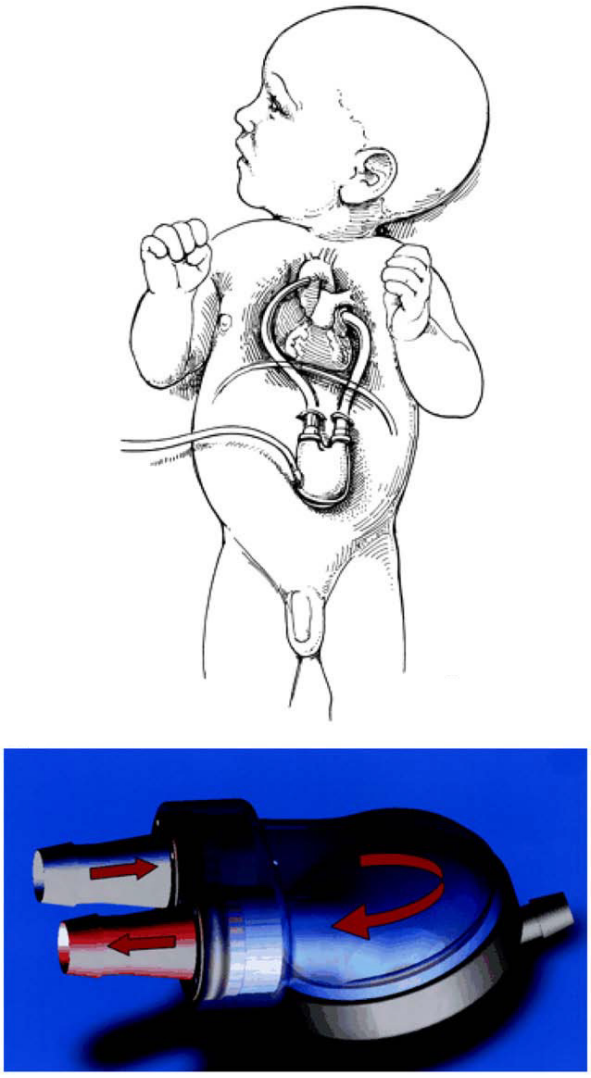

Figure 13 Penn state PVAD (12)

3.7 Levitronix CentriMag Blood Pumping System:

This system is considered as a third generation VAD, manufactured by Levitronix and distributed by Thoratec Corp. CentriMag is an extracorporeal centrifugal pump with continuous outflow, designed for short term support for both adults and small children (20). CentriMag is able to provide support for one ventricle, or both ventricles, it could be also used as a part of the ECMO circuit (27). This pump has received CE mark approval and commercially available in Europe (28).

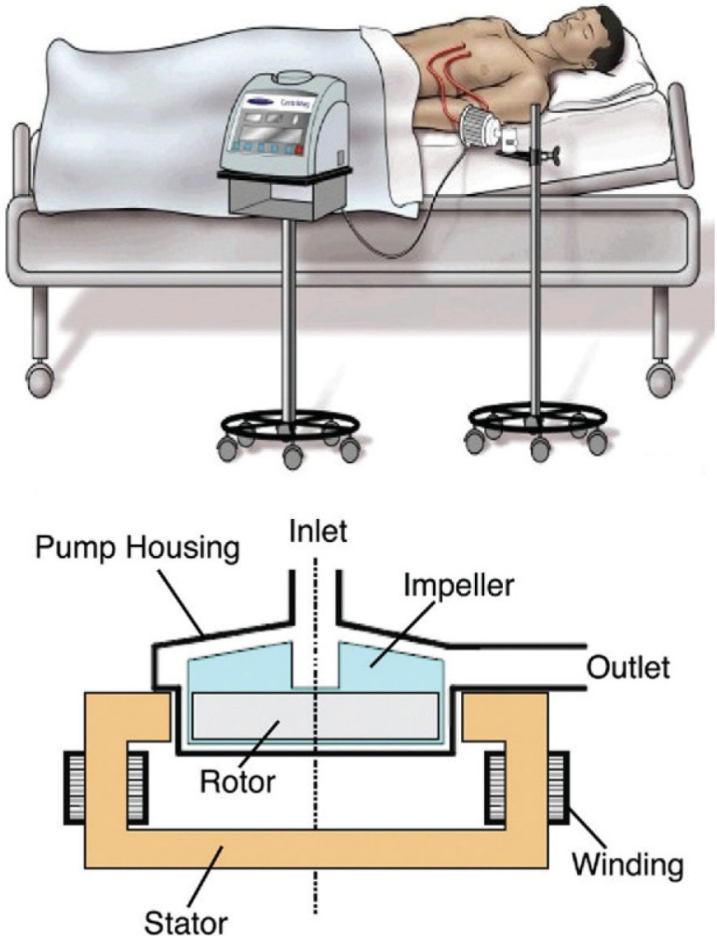

Figure 14 CentriMag (5)

As shown in **Figure -14-**, the pump contains two parts; the rotor which is magnetically levitated located in disposable pump head, and the stator which is a magnet regulated electronically through a processor located in the reusable part of the pump. Blood enters from an inlet at the pump axis and by the centrifugal force leaves at the side. This pump has no mechanical contact which results in less thrombus formation and reduced potential for hemolysis. Pump speed can be controlled from the console, and ranges from 0 to 5,500 RPM, equivalent to flow rates of 0 to 9.9 L/min (20), with a 31 ml priming volume.

Since 2009 Levitronix has been developing a smaller version of CentriMag called PediMag, shown in **Figure -15-**, designed to support infants and small children. It has a 14 ml priming volume, and can provide blood flow of up to 1.5 L/min. PediMag is suitable for short term left ventricular support as BTT, with several reported cases of bridging an infant successfully to transplantation (5).

Figure 15 PediMag (5)

3.8 Levitronix PediVAS:

PediVAS is a special paracorporeal centrifugal pump used to support neonate and pediatric patients, offering short or medium term support duration up to 30 days (20). The pump is capable of providing left ventricular or biventricular support with blood flow ranging from 0.3 to 3.0 L/min at a maximum speed up to 5,000 RPM. PediVAS was reported in supporting the left ventricle in a 3 year old boy with 0.58 m^2 BSA as bridge to recovery, after 3 days the boy started recovering and after 35 days the boy was discharged home (27).

3.9 Tandem Heart:

Tandem Heart **(Figure -16-)** is a paracorporeal centrifugal pump, it is used to support patients >40kg for short durations up to 14 days. This pump has the ability to be connected to the patient's heart either surgically or percutaneously in a catheter lab. It provides 5 L/min in percutaneous position and 8 L/min when it is connected surgically. The pump is magnetically driven, and consists of two chambers; the upper one has the impeller and the lower one has an infusion line to provide anticoagulation for the system (20).

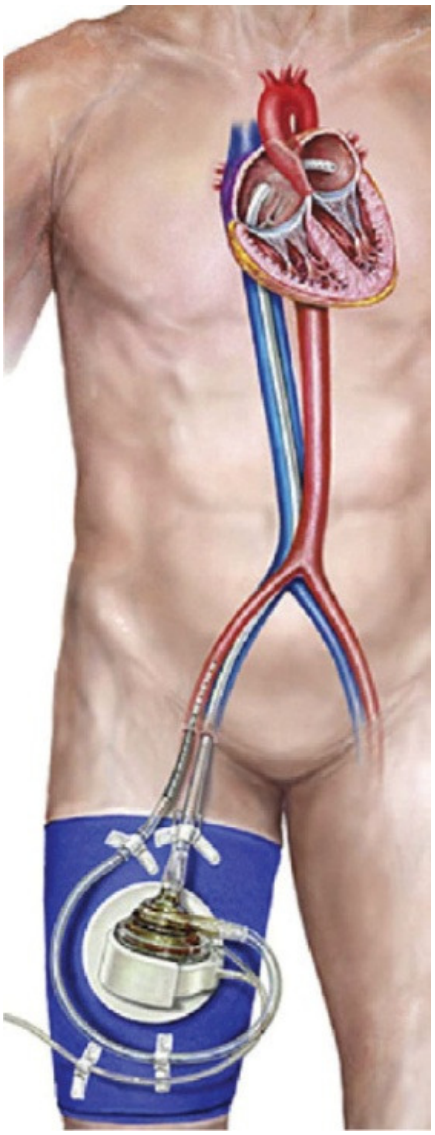

Figure 16 Tandem Heart (20)

3.10 Pediatric pVAD:

The pVAD is a modified version of Tandem heart, developed by Cardio Assist Inc. This new system is designed to support up to 50% of the cardiac output in pediatric patients, and several cannula sizes are available to cover a wide range of patient's size from 3.5 to 50 kg (11).

3.11 Pediatric Cardiac Assist System pCAS:

The pCAS is a paracorporeal rotary flow pump which is combined with an internal oxygenator, shown in **Figure -17-**. This system was developed by Ension Inc., and funding was granted in the first and second phase of the NHLBI program. The rotor part is made from layers of micro porous hollow fibers, and gas exchange occurs through these fibers. Modularity is the main feature of this system, allowing different devices for each patient size to be used. The patient could be moved from the neonate size device to the child size device. Another option that pCAS can offer is pulsatile blood flow at higher heart rates (11).

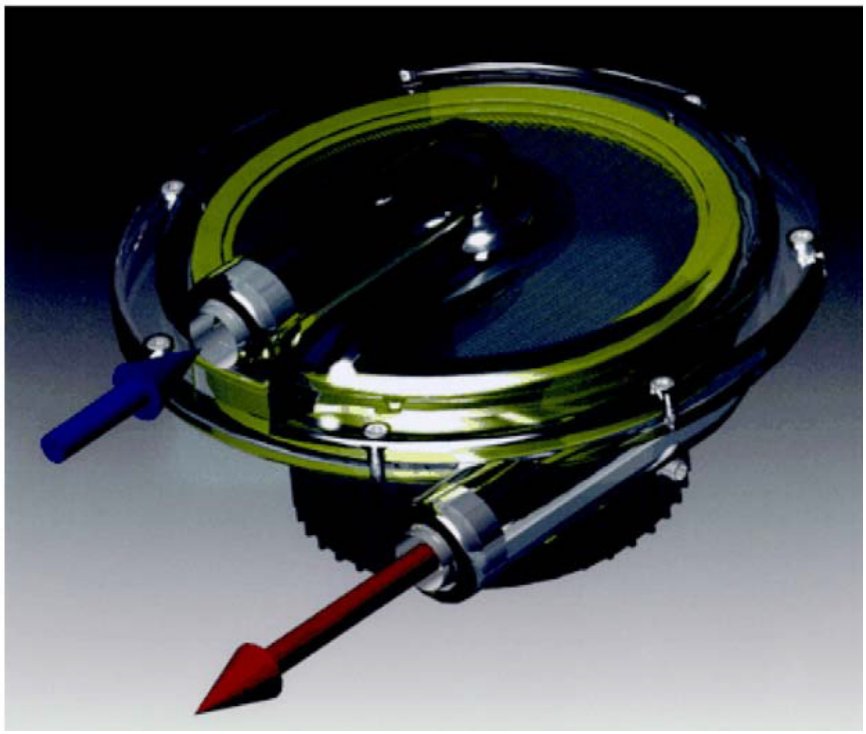

Figure 17 pCAS (12)

3.12 Cardio Flow PQ:

This system is developed by Ension Inc. to provide pulsatile blood flow for neonates. Cardio Flow PQ has almost the same design as pCAS with an internal oxygenator, but it is more oriented towards generating effective pulse pressures at the higher beat rates than pCAS (11).

3.13 Toyobo NCVC LVAS:

Toyobo is a pneumatically driven paracorporeal left ventricular assist system; it is developed by Nipro in Japan. The first use of this device was in 1982, and it became commercially available in 1990. The effective stroke volume is 70 ml, and the maximum output flow is 7 L/min. It has more than 15 years experience in Japan in both adult and pediatric patients (29). One case reported is a 3 year old girl (BSA 0.66m^2, weight 16.2 kg), she was supported successfully to transplantation with Toyobo LVAS, shown in **Figure -18-** (30).

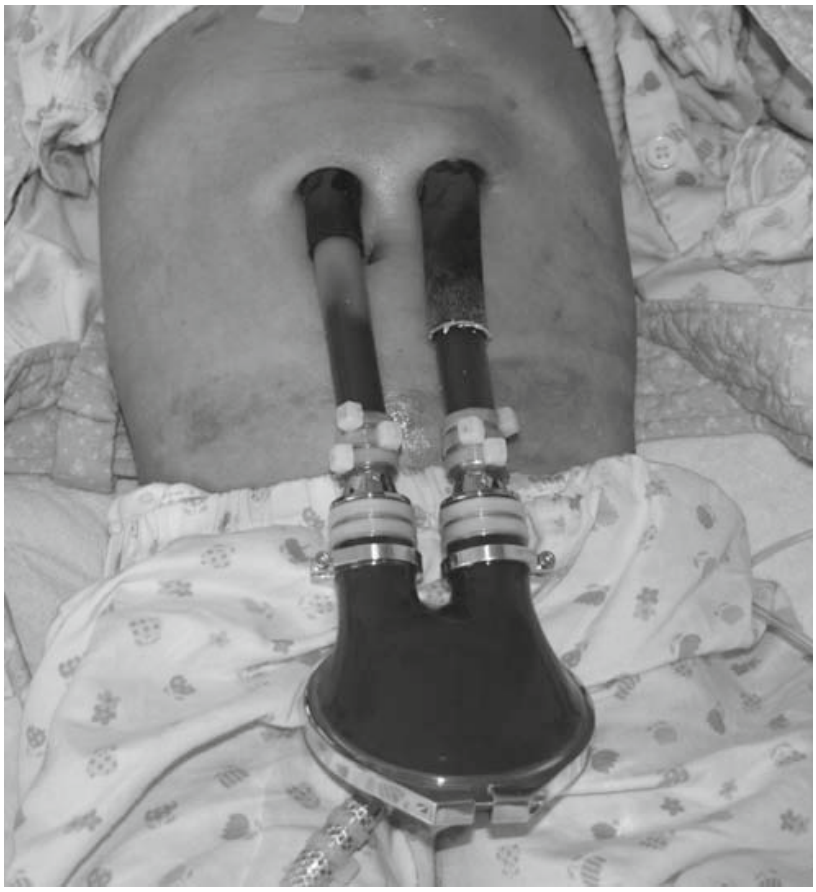

Figure 18 Toyobo LVAS (30)

3.14 Tiny Pump:

Tiny Pump is a small paracorporeal, continuous flow, centrifugal pump, developed since 2004 at Tokyo Medical and Dental University in Japan, and designed to support patients for short durations as BTR or BTT. This low flow pump is designed for neonates and infants between 3 and 15 kg, and can generate blood flow from 0.5 to 1.5 L/min. The pump can also provide higher blood flow up to 4 L/min at 4,500 RPM by using larger cannula, which is enough to support children between 20 and 30 kg. The system measures 20 mm in height, 49 mm in diameter, 150 g total weight and 5 ml priming volume (31).

Figure 19 Tiny Pump (31)

The system consists of a reusable motor, a disposable pump head, and a control consol, **Figure -19-**. The impeller inside the disposable part has six pole magnets, which are coupled with the external magnets in the outer part that are rotated by a DC motor. Blood comes from the left ventricular apex, enters the pump head from the top port, leaves the pump head from the side port, and closes the circulation in the ascending aorta. The disposable pump head is made from polycarbonate, and all blood contacting surfaces are coated with 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer to increase blood compatibility and reduce the risk of thrombus formation. Tiny Pump is still under development. It recently went through in vivo animal testing, and managed to support two goats for two weeks. With the ongoing improvements of this pump, Tiny Pump could be available soon for use in infant and neonate patients (31).

Chapter 4: Intracorporeal Ventricular Assist Devices

VADs that are located inside the patient's body are called intracorporeal VADs. These VADs can be used for small size patients, offering both types of blood flow; pulsatile and continuous. The pump design mainly is based on either axial or centrifugal techniques. Intracorporeal VADs are suitable for longer durations of support than paracorporeal VADs. The main intracorporeal VADs are:

4.1 HeartMate I:

The first generation of HeartMate was manufactured by Thoratec Corp.; three devices were mainly developed in this generation. All of them were implantable, pulsatile pumps, used for medium to long term support as a BTR or DT. They rely, almost all of them, on the same design. A pusher plate pushes a flexible plastic diaphragm against the blood chamber which drives the blood from the left ventricle to the ascending aorta. Two biological porcine valves were used to maintain a pulsatile blood flow. The outer housing is made from titanium (2).

The first one is the HeartMate IP (Implantable Pneumatic). In this model the pusher plate is driven pneumatically by an external compressed air source. It was introduced in 1978, and approved by FDA as a BTR in 1994 (32). The main disadvantages are the use of an external compressed air source which affects the patient mobility and causes a loud noise and the large size of the percutaneous cable going through the patient's skin. The second one is the HeartMate VE (Vented Electric)

which is an enhancement version of HeartMate IP, it was introduced in 1991. The pusher plate in this VAD is driven mechanically by an electric motor that converts the rotary motion of the motor into a linear motion via a ramp and cam mechanism (32).

The third one is the HeartMate XVE (Extended Vented Electric), introduced in 2001, and approved by the FDA in 2003 as a DT, shown in **Figure -20-**. The pusher plate is driven by a similar mechanism to the previous version VE, which reduces the size of the percutaneous cable to 12 mm in diameter for both the electric power cable and the air vent line. This percutaneous cable is covered by woven polyester that encourages skin growth over the tube, and reduces the risk of infection (20). This device measures 110mm x 40mm and weighs 1,190 g which makes it applicable for mono ventricular support only, and suitable for patients with BSA more than 1.5 m^2. HeartMate XVE can achieve 83 ml stroke volume, 10 L/min blood flow at a maximum heart rate of 120 BPM.

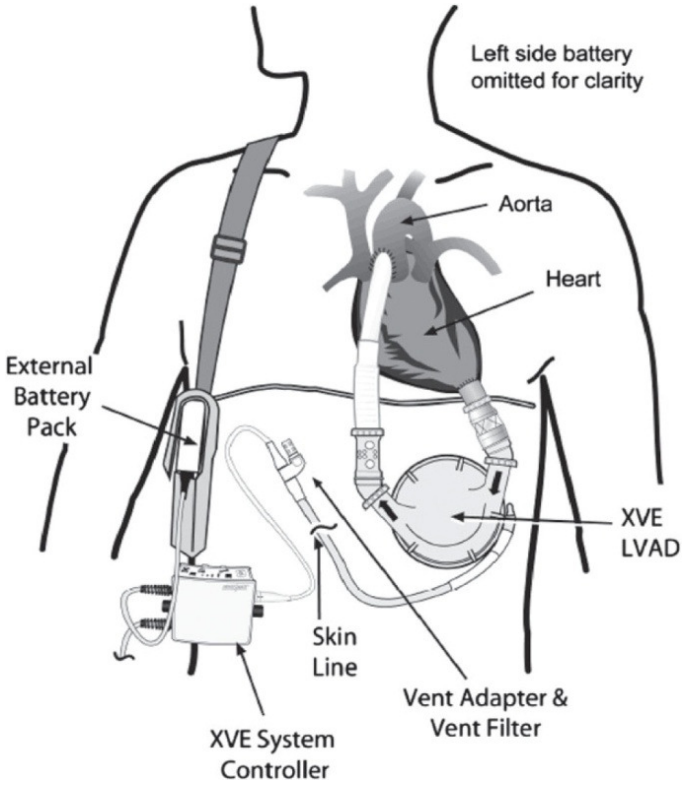

Figure 20 HeartMate XVE (20)

The main advantage of HeartMate XVE is the unique titanium blood contacting surface, which has a sintered surface texture that promotes the formation of a pseudo neo-intima layer, making this surface very similar to a natural blood vessel. This layer reduces the long term anticoagulation therapy required after implantation (32). More than 4,500 patients have received HeartMate XVE, the average duration of support is 100 days, and the longest duration ever recorded was 1,845 days. The system has a small controller which is worn on a belt and the LVAD is powered by portable 2 external battery packs, which allows the patients to move and practice their normal activities with a suitable degree of freedom (13).

HeartMate XVE was used in Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) study. This study focused on the difference between using VADs and conventional medical treatment in end stage heart failure patients. HeartMate XVE showed a 23% survival after 2 years (32).

4.2 HeartMate II:

HeartMate II was firstly developed in 1989 by Nimbus Corporation and University of Pittsburgh, later on Thoratec continued this project and introduced it as the first continuous flow intracorporeal pump produced by Thoratec Corp. . HeartMate II gained approval from the FDA as a BTT therapy in 2008 and a DT in 2010, its design is suitable for long term support. HeartMate II, is an axial flow pump made from titanium, it has just one small moving part (the rotor), unlike the large volume displacement diaphragm pump designs of the HeartMate I, HeartMate II is much smaller, more reliable, and offers better long term support results. This system provides blood flow from 3 to 10 L/min, at a pump speed between 8,000 to 15,000 RPM, measuring 4 cm in diameter and 6 cm in length, the total weight is 370g. HeartMate II recipients range from 9 to 90 years, and BSA from 1.1 to 3.2 m^2, which makes it suitable for small patients like women or adolescents. The pump has a relatively small implantation volume of 63 ml, allowing it to be inserted preperitoneally, or within the abdominal musculature. Two modes of operation are available; the fixed mode RPM between 6,000 and 15,000, and the emergency mode or the power saver mode at 8,000 RPM (33).

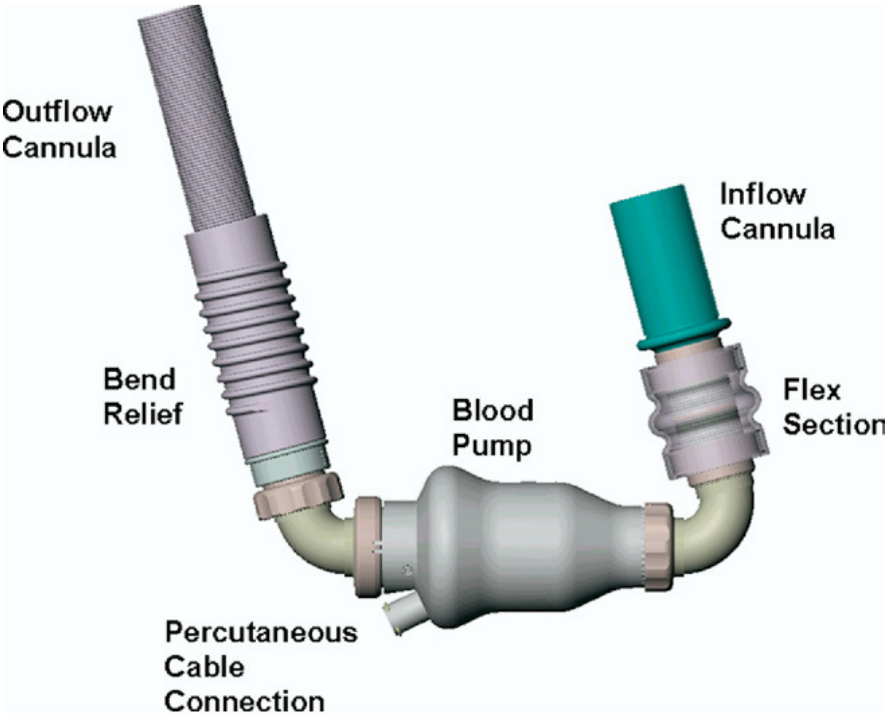

Figure 21 HeartMate II (33)

HeartMate II consists of four main components, as shown in **Figure -21-**: the inflow conduit, the pump, the outflow graft, and the controller. The inflow conduit connects the pump with the left ventricular apex. The conduit is made from woven polyester and is very flexible, allowing it to move freely with the beating ventricle. The pump has a brushless electromagnetic DC motor that provides the rotation to the rotor part. The rotor part has helical blades curved around the central shaft, which spins the blood coming from the left ventricle and moves it to the outflow graft. The rotor has two ruby bearings at each side, and the blood itself is used to cool and lubricate the pump, **Figure -22-** (2). The outflow graft connects the pump with the ascending aorta, the length of this graft can be adjusted to fit each patient's size. The

controller is placed outside the patient's body and is connected to the pump through a small percutaneous cable, **Figure -23-**. The percutaneous cable is covered by woven polyester to encourage skin growth and reduce the risk of infection. The controller is connected to rechargeable batteries worn by the patient, and shows the pump speed and the status of the batteries (13). This small and lightweight controller allows the patients to move and practice their normal activities, and increases the level of possible rehabilitation (34).

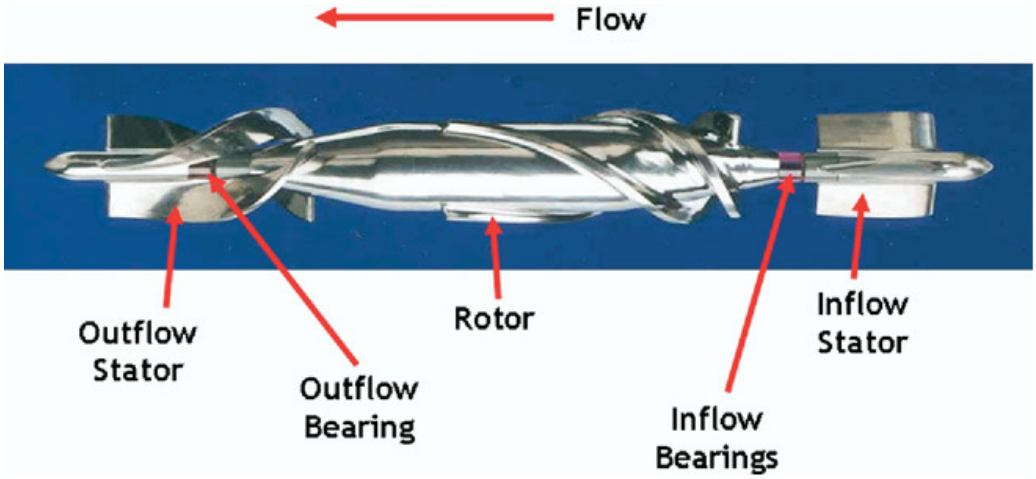

Figure 22 HeartMate II (33)

HeartMate II has the same surface texture of the inflow and outflow grafts as the previous HeartMate I versions. The unique sintered titanium surface was found to reduce the risk of thromboembolic complications after implantation. The specially designed surface stimulates cells to grow on it, eliminating the direct contact between the artificial surface and blood components. More than 6,000 patients have received HeartMate II, 700 patients have been supported for more than 2 years, 60 patients have been supported for

more than 4 years, and the longest duration of continuous support is 6 years.

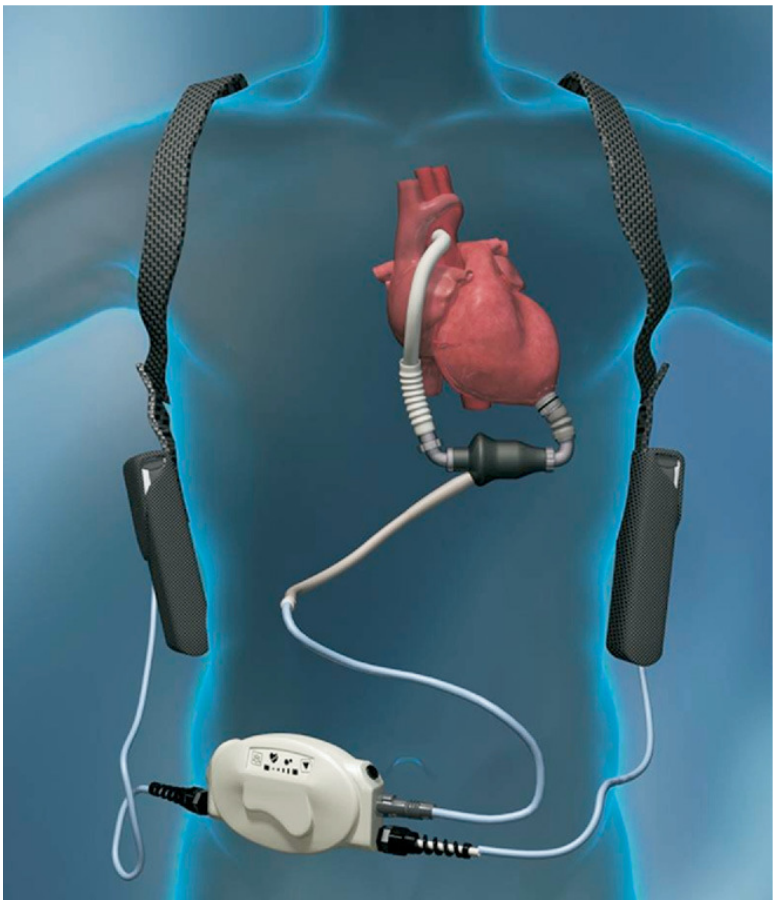

Figure 23 HeartMate II (33)

Like all other continuous axial flow pumps, there is a risk of the negative intraventricular pressure generated by the continuous flow, which can cause the ventricle to collapse. Thus, the position of the inflow conduit is very important to avoid negative pressure (13). Several studies reported using HeartMate II in supporting small size patients. A 12 year old girl with BSA of 1.5 m^2 was diagnosed with dilated cardiomyopathy; she was supported for 85 days with HeartMate II until she received a new heart (34).

4.3 HeartMate III:

Thoratec Corp. is developing a new version of HeartMate VADs based on the 3rd generation pump design. This new VAD is called HeartMate III, and is a compact implantable centrifugal magnetically levitated pump. HeartMate III is a combined system, which has the function of rotation impeller and levitation in one unit. This allows the device to be implanted in a small pocket and is suitable for young children patients as well as adult patients. The device, shown in **Figure -24-**, occupies one third of the HeartMate I in volume and less than three times the volume of HeartMate II, it measures 69 mm in diameter and 30 mm in height, blood flow ranges between 2 to 7 L/min. This small VAD features a very low power consumption, less than 10 W including rotation, elevation, and control (35).

Figure 24 HeartMate III

The design of HeartMate III is based on magnetic levitation technology, where the motor is magnetically connected with the impeller without any direct contact. The pump is made from two parts, the upper one contains the inflow and outflow cannulae, and the lower one contains the motor, shown in **Figure -25-**. Textured titanium housing covers all parts of the pump which, as in all previous versions of HeartMate, helps in reducing thrombus formation. A thin electrical percutaneous cable connects the pump with the main controller and the power source outside the patient's body (35).

Figure 25 HeartMate III

In 2001 HeartMate III went under series of in vivo tests in animal models. It was implanted in 9 calves, 7 cases were supported between 27 and 61 days, with 1 case supported for more than 100 days. The overall performance of the pump was accepted after this test, no mechanical failure occurred and the hemolysis was acceptable (35).

HeartMate III is still under development, and European clinical trials are planned to start by the end of 2012 or the early beginning of 2013.

4.4 Berlin Heart Incor:

Berlin Heart Incor is a continuous axial flow implantable pump, designed for long term support. It was first used in 2002, and received its CE mark in 2003. The Incor design is based on the 3rd generation VAD principle, where the impeller is magnetically levitated without any contact with the stator part, which reduces the risk of wear in the bearings and thrombus formation. This VAD, shown in **Figure -26-**, measures 30 mm in diameter and 120 mm in length, with a total weight of 200 g, and 80 ml volume of implantation (2).

Figure 26 Berlin Heart Incor (2)

The Berlin Heart Incor pump, as shown in **Figure -27-**, consists of a stationary inlet inducer, which brings the blood from the left ventricle apex, and outlet diffuser which delivers the blood back to the ascending aorta, it can provide flow up to 5 - 7 L/min at a rotor speed 8,000 - 10,000 RPM. Power consumption is very low for this system between 2 to 4 W, which ensures that no extra heat is produced by the pump. The magnetic field that lifts the rotor is used to determine the rotor position and this helps in controlling and measuring the pump speed and performance (36). A small percutaneous cable exits the abdominal wall and connects the pump with the controller and power supply source (37).

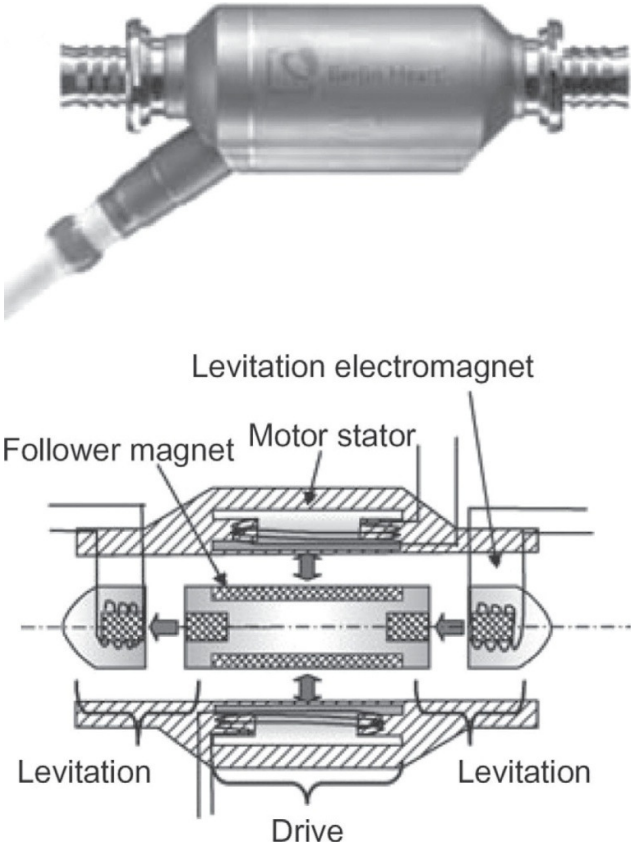

Figure 27 Berlin Heart Incor (36)

All surfaces in contact with blood in this pump are coated with a heparin-bonded film (Carmeda) to improve biocompatibility and reduce thrombus formation. Despite this feature, there are still some problems associated with this pump, including neurological complications due to thromboembolic. The latest design was improved to overcome this problem by modifying the inlet cannula, which was inserted 10 mm inside the left ventricle (2).

Clinical studies reported using this pump in several cases for young children. Since the first use of Incor hundreds of patients have been supported as a BTR or DT, with an average support time of around 146 days, with a maximum recorded duration of 2.5 years (38). 5 children younger than 16 years suffering from dilated cardiomyopathy were supported with Incor VAD as a BTT, the mean duration of support was 53 days, the maximum duration was 420 days (37).

4.5 Thoratec Implantable VAD (IVAD):

The IVAD is a pneumatically driven pump, offering a pulsatile flow. This VAD is the improved version of Thoratec PVAD. It was FDA approved in 2004 as a BTT and BTR for short and medium term support. The device, shown in **Figure -28-**, measures 125 mm x 80 mm x 50 mm and weighs 339 g, allowing the device to be implanted in patients >1.3 m^2 BSA, and offering left, right, or biventricular support (39). This IVAD has a similar design to Thoratec PVAD, with two chambers (one for blood and one for the driving air) separated by a multilayer polyurethane sac. The chamber housing is made of titanium instead of plastic, it is considered as the only option available for biventricular

support. An air compressor is connected to the IVAD through a percutaneous cable, which allows the patient more mobility. The longest duration of using this VAD was 979 days (20).

Figure 28 Thoratec IVAD (2)

4.6 PediaFlow:

PediaFlow VAD is an implantable, magnetically suspended, mixed flow, turbo dynamic blood pump. It was developed by Pittsburgh University in collaboration with Children's Hospital of Pittsburgh, and World Heart Corporation. This system is designed to support pediatric patients from birth to 2 years old with congenital heart problems, weighing between 3 and 15 kg, **Figure -29-** (11).

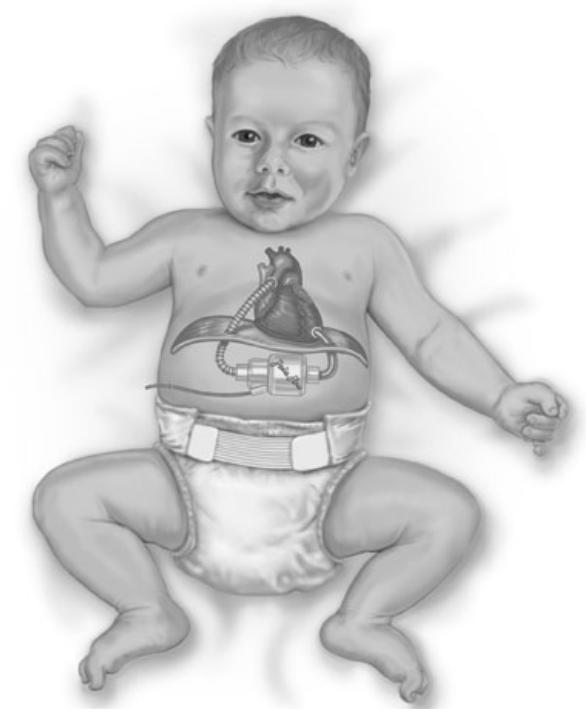

Figure 29 PediaFlow (40)

PediaFlow has a very small size comparing to other pediatric VADs, **Figure -31-**, 51 mm in length, 28 mm in diameter, priming volume is 5 ml, with a total mass of 50 g, blood flow ranges between 0.3 to 1.5 L/min (12). This system can be used as LVAD or RVAD support, and requires just one small percutaneous cable to control the pump and provide the operating power needed. PediaFlow, **Figure -30-**, is a fully magnetically levitated rotor pump with no contact bearings or seals, this means there are no stagnation areas, or high shear force that cause hemolysis or thrombus formation. Using a bearingless pump design in this implantable VAD eliminates the risk of wearing between the contacting surfaces, and increases the operating life time of the pump (40).

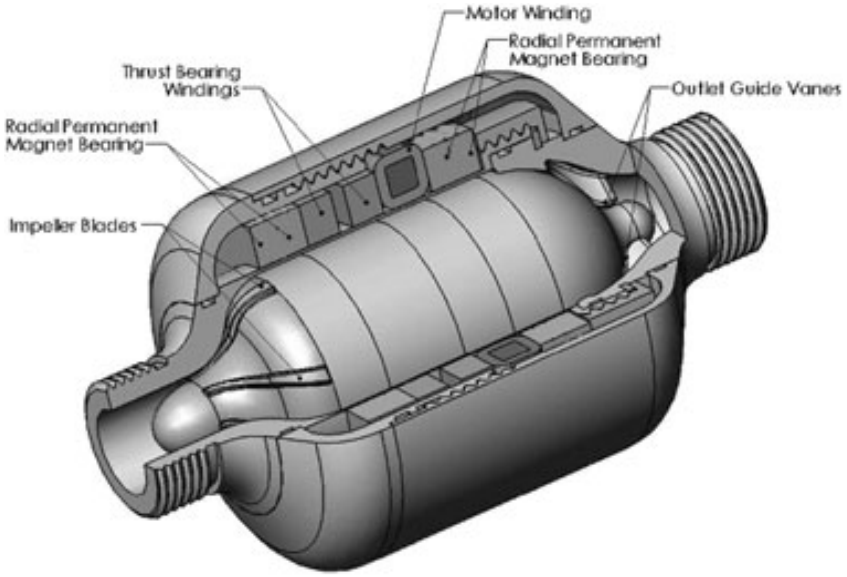

Figure 30 PediaFlow (40)

In 2004 PediaFlow was awarded by the NHLBI program first phase, and it was the only fully magnetically levitated rotor pump participating in this program. In 2009 the second phase of NHLBI program started. Several problems need to be solved in this phase of the study, such as the degree of anticoagulation required. PediaFlow still needs to go through series of tests, including in vivo evaluation, before being able to be implanted in patients (5).

Figure 31 PediaFlow (5)

4.7 Micromed DeBakey VAD Child/ Heart Assist 5:

Micromed DeBakey VAD Child (or currently known as Heart Assist 5) is a totally implantable, axial flow, electromagnetic pump, which has been developed since 1988 by the Baylor College of Medicine and NASA. This system is designed to assist the failing heart of pediatric patients between 5 and 16 years old, with BSA between 0.7 and 1.5m^2. It received FDA approval in 2004 as a BTR for end stage heart failure patients (1). The DeBakey VAD Child was developed from the adult size VAD after some changes to make it suitable for small size patient, those changes are: shortened inflow and outflow cannulae, more acute angle in the inflow tube, and reduced size of the flow probe. This device, shown in **Figure -32-**, measures 30 mm in diameter, 76 mm in length, and the total weight is 95g (41).

Figure 32 DeBakey Child VAD (41)

The DeBakey Child VAD consists of four main components: the implantable pump, the external controller, the external clinical data acquisition system, and the external home support system. The

implantable pump has three main parts: the titanium inflow cannula that connects the ventricular apex with the pump. The main pump which is made from titanium, and provides continuous blood flow by the rotating impeller, **Figure -33-**. The outflow Vascutek Gelweave graft that connects the pump with the ascending aorta (12). Blood flow is measured by an ultrasound flow probe placed in the outflow graft. The probe is connected with the external controller by a small percutaneous cable. This system is implanted in the pericardial space, not inside the ventricle. The pump can provide blood flow up to 5 L/min at a pump speed up to 10,000 RPM (20).

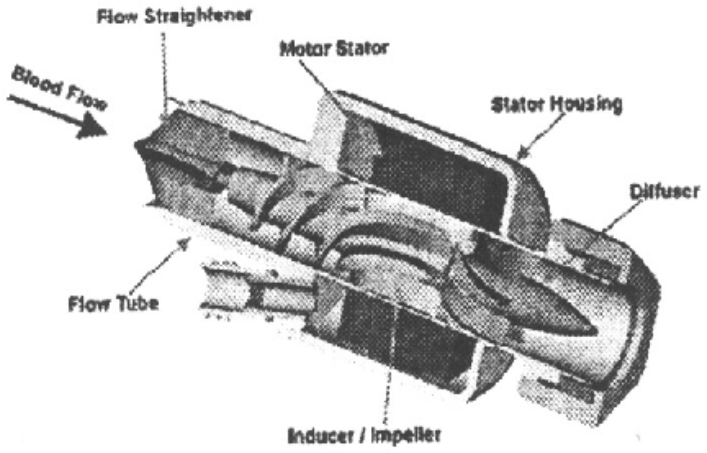

Figure 33 DeBakey Child VAD (1)

Although the number of clinical trials is limited with DeBakey Child VAD, this VAD shows good results in the initial multicentre studies. The longest duration of support using DeBakey Child VAD is 518 days (38).

4.8 Infant and Child Size Jarvik 2000 VAD:

Infant and Child size Jarvik 2000 is an implantable, continuous axial flow pump. This VAD was developed from the adult size Jarvik 2000 by Dr. Robert Jarvik at Jarvik Heart Inc., and is designed for medium to long term support as a BTR or DT. Jarvik 2000 VAD was first available for adult patients, and the first successful VAD implantation was in 2000. It measures 25 mm in diameter, 55 mm in length, and weighs 85 g. Two other versions are now under development for infants and small children, **Figure -34-**.

Figure 34 Jarvik 2000 (12)

The pump consists of a brushless DC motor, a rotor supported on 2 ceramic bearings, and a spinning titanium impeller, all placed inside a titanium shell, **Figure -35-**. The motor creates an electromagnetic force that forces the impeller to spin and push the blood from the left ventricular apex through the outflow conduit to either the ascending

aorta or descending aorta **Figure -36-**. This electromagnetic motor spins the impeller at 8,000 to 12,000 RPM, which generates blood flow of between 3 and 7 L/min, with power consumption less than 8 W. All blood contacting surfaces inside the pump are made of smooth surface titanium to reduce the risk of thrombus formation (33). The pump is connected to an external controller and power source by a percutaneous cable through the abdominal wall. This cable is partially coated with Dacron to reduce the risk of infection (20).

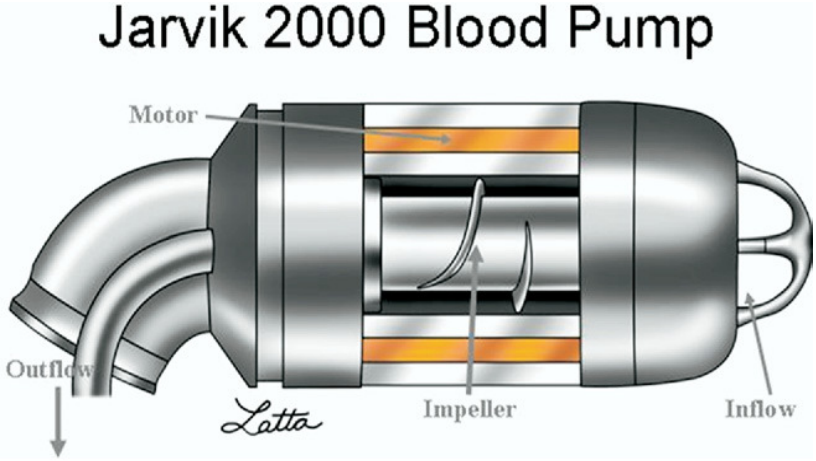

Figure 35 Jarvik 2000 (33)

The device is available in two different sizes. The first one is the child size VAD with 10 ml priming volume, 35 g weight, which makes it suitable for small children between 15 and 25 kg. The second one is the infant size VAD with 4 ml priming volume, 12 g weight, used for infants between 3 and 15 kg. Due to its special design and small size, Jarvik VAD can be implanted inside any chamber of the heart (11).

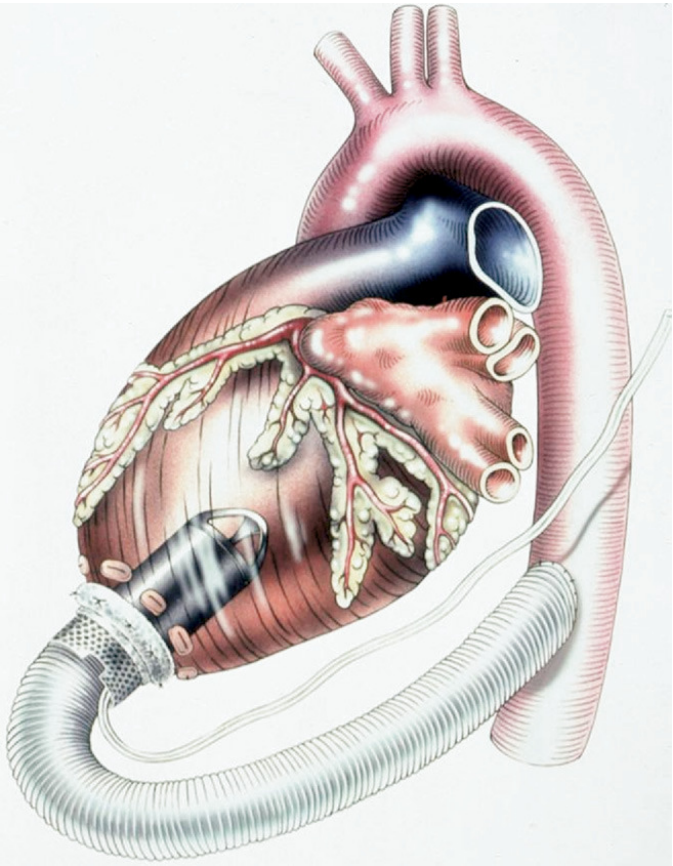

Figure 36 Jarvik 2000 (33)

More than 300 patients have been supported with Jarvik 2000 VAD for adults since the first use in 2000. Peter Houghton was the longest surviving cardiac patient supported by a mechanical heart; he used Jarvik 2000 VAD for 7.5 years without any problems during that time. Although the Jarvik 2000 VAD has two mechanical bearings, no mechanical failures have been recorded since the first use of this VAD. All these clinical experiences and positive results give good signs for the new Jarvik 2000 Child VAD in the near future (42).

4.9 PediPump:

PediPump is an implantable, axial flow VAD, the design is based on the Cleveland Clinic adult size pump. In 2004 PediPump was developed under the NHLBI first phase program, it is able to provide left ventricular, right ventricular, or biventricular support. This new VAD is suitable for small size patients from newborns to adolescents, ranging from 2 to 25 kg. PediPump is magnetically levitated without any mechanical bearings or seals; this increases the pump life time and durability and reduces the risk of clot formation. The pump, as shown in **Figure -37-**, consists of an impeller with three blades lifted magnetically from both sides, and an electric motor with magnets in the center. All components are placed inside a titanium shell (43).

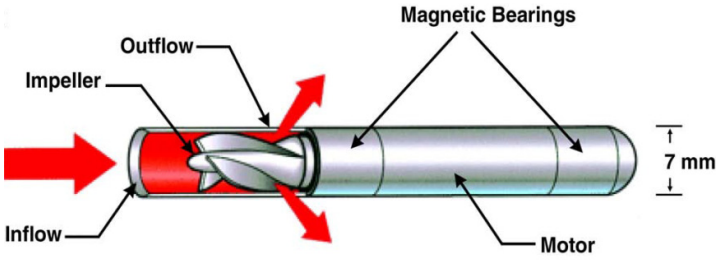

Figure 37 PediPump (12)

PediPump is a very small VAD, measures just 7 mm in diameter, and 60 mm in length, with a 0.6ml priming volume. This VAD, as shown in **Figure -38-**, can be implanted in the intraventricular mode for patients less than 15 kg, where the pump can fit inside the aorta for LVAD support or inside the pulmonary artery for RVAD support. For patients more than 15 kg it can be implanted in the extraventricular

mode, where the inflow conduit is connected to the left ventricular apex and the outflow graft is connected to ascending aorta (11).

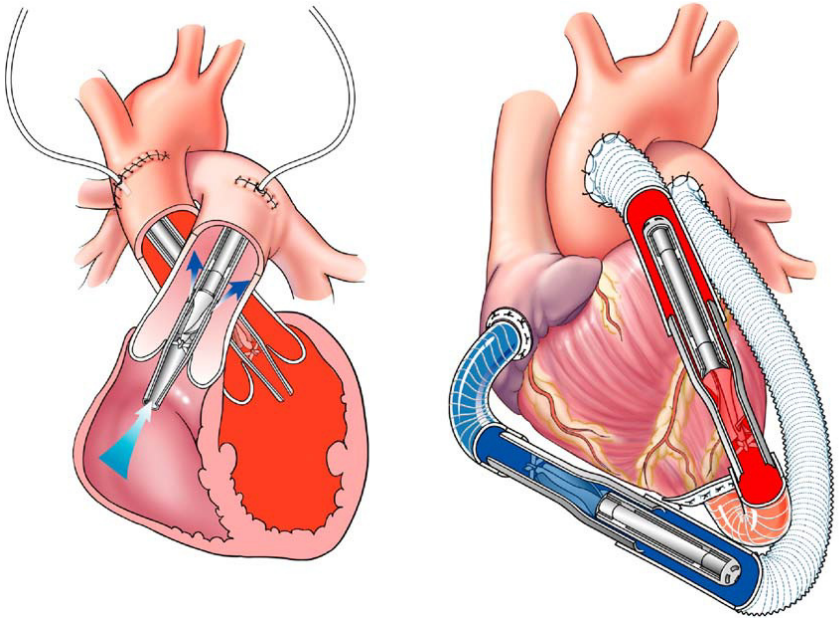

Figure 38 PediPump (11)

Cleveland Clinic is still developing PediPump VAD; a new version of PediPump is called Mark III. The improvements in Mark III were in magnetic bearing design, motor design, wash flow path, axial touch point design, and electrical / thermal insulation. The current version of PediPump is called Mark IV which has all the previous improvements in Mark III plus a reduction in the axial length of the pump (44).

4.10 Toddler VAD:

Pittsburgh University in collaboration with Carnegie-Mellon University is developing a small implantable VAD, in a project called the Toddler VAD. Toddler VAD, shown in **Figure -39-**, is designed to support small children between 15 and 35 kg, and is able to provide full cardiac support for 3 months. The pump design is based on a mixed-flow type

pump with magnetic bearings, blood is used to lubricate and cool the pump (11).

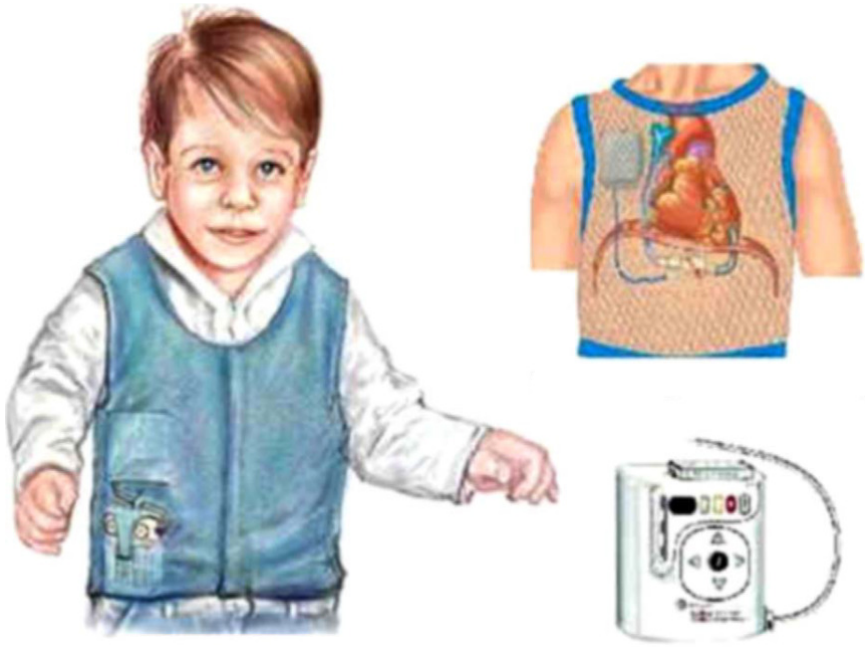

Figure 39 Toddler VAD (11)

4.11 CorAide:

The CorAide is an implantable centrifugal pump, developed by Cleveland Clinic. This pump, **Figure -40-**, has just one moving part, the rotating assembly, which is supported by hydrodynamic bearings and a passive magnetic axial reaction. A few patients have been supported with CorAide VAD in Europe without any problems (38).

Figure 40 CorAide VAD (38)

4.12 Levacor VAD:

Levacor VAD is an implantable, centrifugal, 3rd generation continuous flow pump, developed by World Heart Corporation. This VAD is designed for long term left ventricular support. Levacor VAD, as shown in **Figure -41-**, is not a very small VAD, measuring 35 mm in height and 75 mm in diameter. It has a 75 ml priming volume, and is heavier than other axial flow VADs at a weight of 440 g, which makes it only applicable for large or medium size patients (36).

Figure 41 Levacor VAD (36)

The magnetic levitation system consists of two magnets; the permanent magnet that provides passive levitation, and the electric magnet that provides active levitation. Both active and passive magnet bearings provide completely suspension of the centrifugal impeller. These magnetic bearings limit wear and increase the VAD life time. The device can provide blood flow in the range between 0 and 10 L/min. All blood contacting surfaces are polished titanium to increase blood compatibility and limit thrombus formation. Only a few patients have been supported with Levacor VAD in Canada and Europe, and successful results were reported from the clinical centers there. In the USA the device is still under investigation, since 2006 (2).

4.13 Circulite Micro VAD:

The Circulite Micro VAD is a miniature implantable rotary pump, designed to offer medium to long term support of the failing heart as a BTR or DT, suitable for both children and adult patients. This VAD is considered the smallest and lightest VAD, **Figure -42-**, measuring just 12mm in diameter, 50 mm in length, with 1.5 ml priming volume, and 25 g mass. The small size of this VAD allows it to be placed in a chest wall pocket similar to a pacemaker pocket with less invasive surgery (2).

Figure 42 Circulite Micro VAD (2)

Circulit Micro VAD has a mixed flow impeller suspended on a pivot bearing. The impeller can produce blood flow up to 3 L/min at 28,000 RPM, offering partial support for blood circulation. All components are placed in titanium housing. The new feature in this VAD is the anatomical connection method, where the inflow cannula is connected to the left atrium, and the outflow one is connected to the subclavian artery. This new technique in cannulation has reduced the typical left ventricular apical trauma and the workload of the heart, which results in providing suitable condition for the heart to recover (2).

After short term testing in animals, no signs of hemolysis or embolic were found, and long term studies are still in process. CE clinical trials started in 2007 in Europe, and more than 27 patients have been supported by Circulite Micro VAD (11).

4.14 Dura Heart:

Dura Heart is an implantable continuous flow rotary pump, developed by Terumo Corporation. This VAD is relatively large at 72 mm in diameter, 45 mm in height, and weighs 540g, **Figure -43-**. This VAD is suitable for patients BSA > 1.5 m^2, and is able to provide long term left ventricular support. The first implant was in 2004, CE mark obtained in 2007 (2).

Figure 43 Dura Heart VAD (36)

Dura Heart is based on 3rd generation pump design. A rotational impeller is suspended by magnetic bearings placed in the upper chamber of the system, and a DC motor is placed in the lower chamber of the system. This motor provides impeller speed from 1,200 to 2,600 RPM, producing blood flow between 2 and 10 L/min. All pump components are placed inside titanium housing, coated with covalently bonded heparin which prevents thrombus formation inside the pump (36).

4.15 VentrAssist:

VentrAssist is an implantable 3rd generation centrifugal VAD, designed to assist the heart for short or long term basis as a BTT or DT. It was developed by Australian researchers in 1999. The device weighs 298 g, and measures 60 mm in diameter (36).

The system consists of a small blood pump placed in small pocket in the left side of the body below the diaphragm, shown in **Figure -44-**. This pump is attached with the left ventricular apex through an inlet cannula, and another outflow cannula is connected to the ascending aorta. The internal pump is connected to the external controller and power source by a small percutaneous cable exiting the body from the upper right quadrant. This external controller is powered by rechargeable batteries, indicates system parameters such as pump speed and status of the batteries, and includes audible and visible alarms. The operating range is between 1,800 and 3,000 RPM.

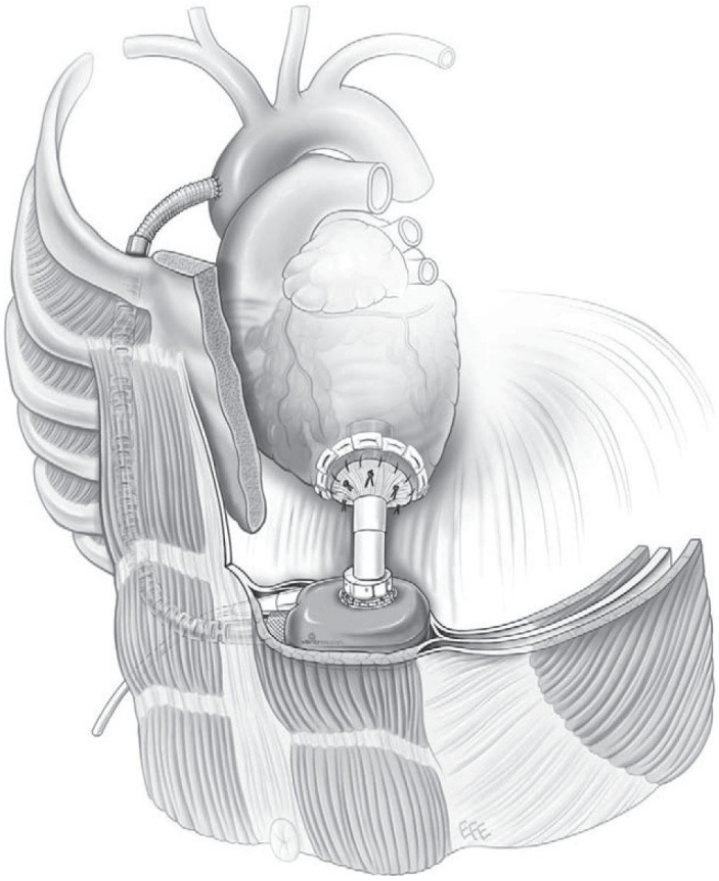

Figure 44 VentrAssist VAD (45)

Pump design is based on the 3rd generation impeller system, where the impeller is magnetically levitated without any mechanical bearings. In this type of bearing the frictional wear and blood flow obstruction are eliminated; the risk of clot formation is also reduced to the minimum. The impeller has four blades, **Figure -45-**, all of which have permanent magnets inside, sequentially switching on and off the electric current between three pairs of coils, causing the blades to spin and direct the flow. Titanium housing covers all the components of the pump. The unique feature of this design is the use of Diamond Like Carbon material to coat all blood contacting surfaces, which reduces

platelet adhesion on the surfaces and minimizes thrombus formation (46).

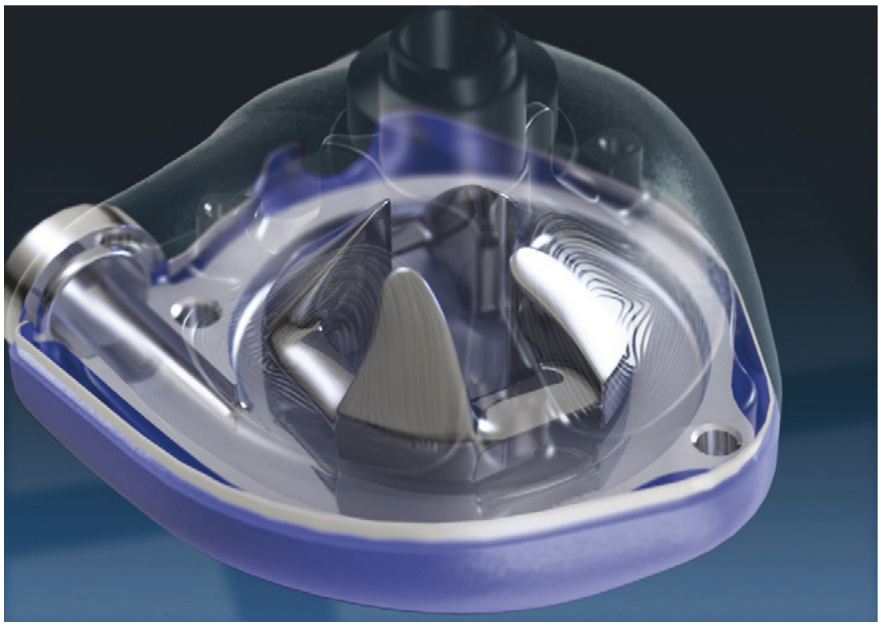

Figure 45 VentrAssist VAD (46)

The initial clinical studies started in 2003 in Australia and Europe, and continued in the USA as part of the FDA approval requirements. Several cases have been reported using this VAD since the beginning of the clinical trials. A 14 year old girl suffering from dilated cardiomyopathy was supported with VentrAssist VAD as a bridge to transplantation. The maximum duration of support ever recorded with VentrAssist VAD is 2.7 years (47).

4.16 Novacor LVAS:

The Novacor LVAS is an implantable pulsatile flow pump, designed by World Heart in 1984 as a bridge to transplant, and FDA approved in 1988. The pump design is based on a pusher plate to provide pulsatile flow, and two biological valves used to maintain the

flow in one direction. The pusher plate is driven by an electrical solenoid, which is connected with an external power source through a percutaneous cable. Blood enters the pump through the inflow conduit, coming from the left ventricular apex, and leaves through the outflow one to the ascending aorta. The entire assembly, as shown in **Figure -46-**, is encased in lightweight epoxy housing, the total weight of this system is 850 g (32).

Figure 46 Novacor LVAS

Novacor II is the new version, featuring a magnetically actuated pusher plate. The main advantage of this VAD that it does not need any compliance chamber or venting line. Novacor II is still under development, but the new version will be totally implantable, including batteries and controller system (20).

More than one thousand patients have received Novacor since the first use. 3 patients survived over 4 years, 9 patients over 3 years, and 26 patients over 2 years. Some problems have been recorded regarding thromboembolic events and the intense permanent anticoagulation therapy needed (48).

4.17 Heart Ware Ventricular Assist Device HVAD:

HVAD is a small implantable centrifugal radial flow pump. Developed by Heart Ware Inc., pump design is based on the 3rd generation technique. HVAD is one of the smallest 3rd generations VAD, **Figure -47-**, measures 53 mm in diameter, weighs 140g, and 50 ml displacement volume, it can be placed in the pericardial cavity without any need to make a preperitoneal pocket. This VAD is suitable for both adult and children patients. It was first designed for left ventricular support but later modified for Biventricular support. CE mark was obtained in 2009, and FDA trials are still in progress (2).

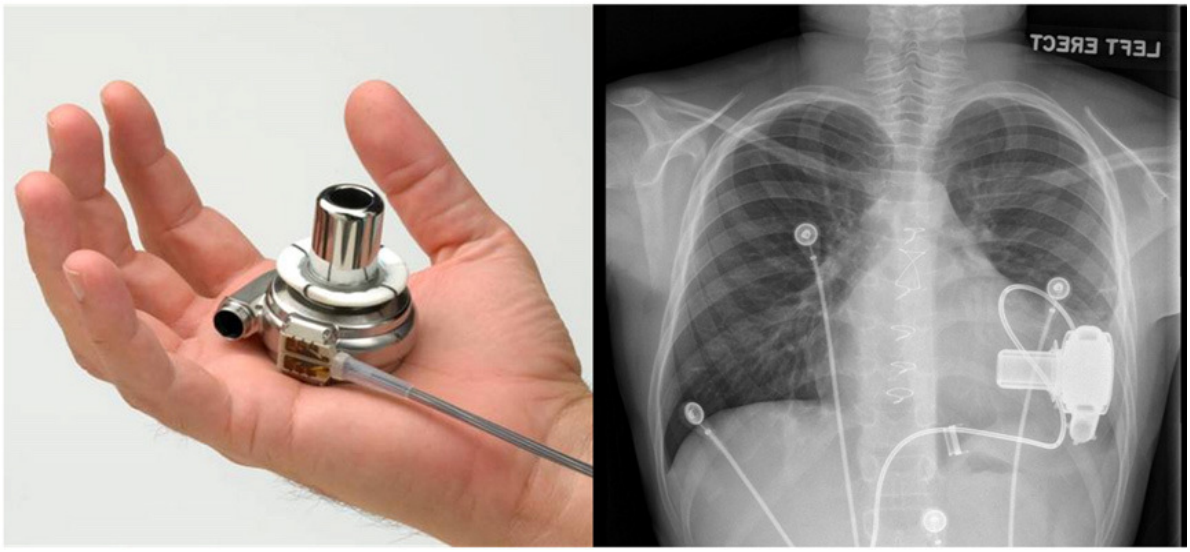

Figure 47 HVAD (5)

The HVAD pump is located inside titanium housing, **Figure -48-**; it has one moving part, the impeller, which is magnetically suspended by passive magnetic and hydrodynamic forces. HVAD has two integrated cannulae; the inflow cannula connects the pump with the left ventricle, and the outflow connects the pump with the ascending aorta. This pump can provide blood flow up to 10 L/min at pump speed between 1,8000 and 4,000 RPM. The pump is connected with an external power source and controller through a flexible percutaneous cable, which is coated with polyurethane to minimize the risk of infection. The external controller monitors all pump parameters and the status of the power source (49).

Figure 48 HVAD (13)

Clinical trials began in 2008, and showed that HVAD is a highly reliable VAD. More than 700 patients have received HVAD (13). A German group has reported using HVAD to bridge a boy to transplantation successfully. A 10 year old suffering from dilated cardiomyopathy has been supported successfully also in the USA (5).

4.18 Abiomed Impella cVAD:

The Abiomed Impella is the smallest intravascular micro axial blood pump, offering partial support for up to 6 hours. The Impella pump is mounted on a catheter, available in two sizes; 12F offering 2.5 L/min blood flow support, and 21F offering 5 L/min blood flow support. It is percutaneously introduced in a catheter lab through the femoral artery into the left ventricle. The pump consists of the inflow port that is placed in the left ventricle under the aortic valve, **Figure -49-**, an encapsulated axial motor, and the outflow port that ejects the pumped blood into the ascending aorta. Impella can be applied for either left or right ventricular support. The Impella 2.5 is FDA 510(k) approved for short-term circulatory support (50). However, percutaneous approaches for supporting the circulatory system can have significant complications, such as excessive bleeding or limb ischemia.

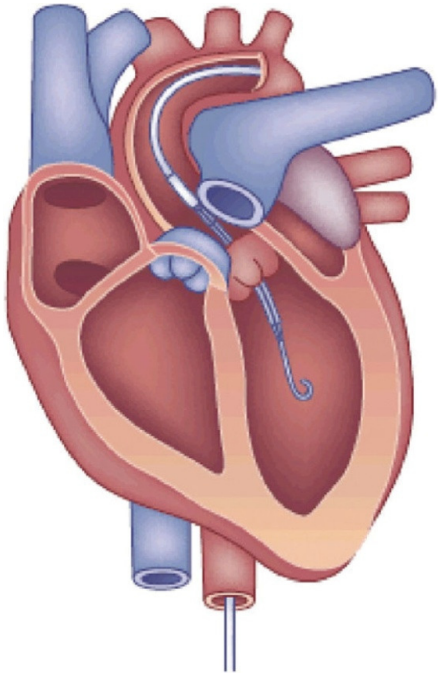

Figure 49 Abiomed Impella cVAD (20)

Chapter 5: Summary and Discussion

5.1 VAD and ECMO:

Extracorporeal Membrane Oxygenation (ECMO) was the first option available to offer cardiac support for pediatric patients in the early days. Offering both cardiac and respiratory support is the main advantage of using ECMO. It is also relatively easy in installation and cannulation, and there is a long history of experience associated with this type of treatment in the pediatric field. On the other hand, the complicated blood circuit, the need of intense anticoagulation therapy, and the high risk of infection are the major limitations of applying ECMO. Nonpulsatile blood flow still has unknown effects on the microcirculation perfusion of some organs such as the brain, lungs, liver and kidneys, clinical studies are still in progress focusing on this issue. Mobility restriction is another problem for ECMO patients, where the patient receiving ECMO support is totally paralyzed and cannot move at all. In the long term support this will have bad consequences on the patients who will need physical rehabilitation after recovery (12).

On the other side, VADs have been invented to overcome these limitations and restrictions of ECMO. VADs offer a wide spectrum of options for almost all cases. VADs are now available for all patient size from neonates to adults, offering full cardiac support or partial support. They are suitable for short duration use as a bridge to recovery or as a bridge to transplantation, and long term use as a destination therapy. They can be totally implanted inside the patient's body (intracorporeal) or located outside the patient's body (extracorporeal) and in both case

they can offer various degrees of freedom and mobility. Pulsatile and continuous blood flow devices are both available depending on the design of the pump, and in some new VADs they can even switch between pulsatile and continuous blood flow depending on cardiac output. VAD is still a new and expensive option, costing around $150,000 for the device and the surgery. Some of the new devices are still under development and still require long clinical experience before being accepted.

5.2 VADs Generations:

5.2.1 1st Generation VADs:

The first generation design is based on a pulsatile positive displacement pump. This engineering design consists of an internal blood chamber, two mechanical or biological valves to maintain unidirectional blood flow, and two grafts for inflow and outflow. The pump is either driven pneumatically by an external compressed air source, or by electric mechanical actuator driven by an internal electric motor. These latter devices are big, heavy, noisy, and they need large percutaneous cables, which incorporates an air vent line to equalize the atmospheric pressure in the motor chamber. There is also a high incidence of mechanical failure associated with long term support. All these limitations restrict the use of 1st generation VADs for young children, and are not suitable for pediatric patients (36).

5.2.2 2nd Generation VADs:

The second generation design is based on a continuous flow rotary pumps which are suspended on contact bearings. These VADs

contain two main parts the rotor and the stator, beside also two grafts for inflow and outflow. The rotor is pivoted on two mechanical bearings at each end of the rotor spindle, with spinning of the rotor achieved by magnetic coupling with the motor placed in the stator part. A thin percutaneous cable exits the body and connects the device with an external electrical power source and system controller. The 2nd generation VADs is much smaller, lighter, and quieter than the 1st generation. This allows them to be implantable for small patients and adults, and suitable for medium and long term support (36).

5.2.3 3rd Generation VADs:

The third generation design is based on a continuous flow rotary pumps which are suspended on noncontact bearings system. This design is very similar to the 2nd generation devices, except for the bearing mechanism. The pump consists of two parts (the stator and the rotor), the latter part being suspended magnetically within the stator part. This levitation force could be either passive (depending on a permanent magnets), or active (generated by an electrical current passing through a coil). In both cases this technique helps in reducing the power consumption. These noncontact bearings reduce the risk of flow stagnation, thrombus formation, heat generated by friction, and mechanical wear (36).

The 1st, 2nd, and 3rd generation VADs are listed in **table -1-** below:

1st Generation	2nd Generation	3rd Generation
HeartMate I	HeartMate II	HeartMate III
Thoratec Implantable VAD (IVAD)	Micromed DeBakey VAD Child/ Heart Assist 5	Berlin Heart Incor
Thoratec PVAD	Infant and Child Size Jarvik 2000 VAD	PediaFlow
Berlin Heart EXCOR	Circulite Micro VAD	PediPump
MEDOS HIA VAD	Abiomed Impella cVAD Tandem Heart	Toddler VAD
Novacor LVAS	Pediatric pVAD	CorAide
Abiomed Biventricular Support 5000	Pediatric Cardiac Assist System pCAS	Levacor VAD
Abiomed AB 5000	Cardio Flow PQ	Dura Heart
Penn State PVAD		VentrAssist
Toyobo NCVC LVAS		Heart Ware Ventricular Assist Device HVAD
		Levitronix PediVAS
		Tiny Pump
		Levitronix CentriMag Blood Pumping System

Table 1 VADs Generations

5.3 Intracorporeal and Extracorporeal VADs:

Extracorporeal pumps are the early VADs used to support pediatric patients, offering less mobility restriction than ECMO, and longer time than previous options. This type of VAD is used for short to medium term support until heart recovery or transplantation. The patient with extracorporeal VAD should stay at the hospital all the time for monitoring. The location of the VAD outside the body allows easy monitoring of the blood flow and helps in observing any kind of thrombus formation; any mechanical failure could be directly noticed and solved immediately. The main disadvantage is the high risk of infection due to the large tubes needed to connect the pump with the patient's heart; 2 tubes for single ventricular support and 4 tubes for biventricular support. Special care is needed to keep these tubes clean and sterilized at the skin entry sites.

The other type of VAD is the intracorporeal VAD, where the pump is fully implanted inside the patient's body either intraventricular or extraventricular, depending on the size of the pump and the patient. This type is able to provide either short term or long term support. Unlike the extracorporeal VADs there is no need for any external motor or air compressor, the intracorporeal pump is just connected to a small controller and a set of rechargeable batteries through a thin percutaneous cable. This small percutaneous cable helps to reduce the risk of infection. Patients with intracorporeal VADs can move very easily and leave the hospital after implantation.

Intracorporeal and Extracorporeal VADs are listed in **table -2-** below:

Intracorporeal VADs	Extracorporeal VADs
HeartMate I	Thoratec PVAD
HeartMate II	Berlin Heart EXCOR
HeartMate III	MEDOS HIA VAD
Berlin Heart Incor	Abiomed Biventricular Support 5000
Thoratec Implantable VAD (IVAD)	Abiomed AB 5000
PediaFlow	Penn State PVAD
Micromed DeBakey VAD Child/ Heart Assist 5	Levitronix CentriMag Blood Pumping System
Infant and Child Size Jarvik 2000 VAD	Levitronix PediVAS
PediPump	Tandem Heart
Toddler VAD	Pediatric pVAD
CorAide	Pediatric Cardiac Assist System pCAS
Levacor VAD	Cardio Flow PQ
Circulite Micro VAD	Toyobo NCVC LVAS
Dura Heart	Tiny Pump
VentrAssist	
Novacor LVAS	
Heart Ware Ventricular Assist Device HVAD	
Abiomed Impella cVAD	

Table 2 Intracorporeal and Extracorporeal VADs

5.4 Continuous Flow and Pulsatile Flow:

Pulsatile flow or positive displacement pumps are the first generation VAD's pumps. Pulsatile flow pumps are either pneumatically or electrically driven pumps. Pneumatic pumps need an external compressed air source to push the diaphragm, while the electrical pumps have an electrical motor to drive the pusher plate. Those pumps are very large in size, which make them unsuitable for small patient sizes. They need a large vent line for the pusher plate chamber, which increases the risk of infection. On the other hand, this type of pump has a simple control system and can be adjusted very easily to accommodate with the patient's need for everyday activities (38).

The vast majority of VADs available for pediatric patients are continuous flow pumps; there are two types as previously described, the axial pumps and the centrifugal pumps. Both axial and centrifugal pumps have almost the same design; a rotor impeller is generating the flow. In the axial flow, the impeller is in the same line of the inflow and outflow tubes, whereas in the centrifugal pump the inflow cannula is in the top of the pump and the outflow one is coming from the side of the pump. Centrifugal pumps have the advantage of less ventricular suction which reduces the risk of left ventricular collapse (38).

In general continuous flow pumps have the following advantages: small in size, quiet, no need for valves, no need for vent lines, a thin drive line or percutaneous cable, and very low power consumption. Very complicated control mechanism, inability to respond to the flow

rate needed by the patient, and the unknown outcomes of nonpulsatile flow are the main disadvantages of continuous flow pumps (38).

Continuous flow and pulsatile flow VADs are listed in **table -3-** below:

Continuous Blood Flow VADs	Pulsatile Blood Flow VADs
HeartMate II	HeartMate I
HeartMate II	Thoratec PVAD
Berlin Heart Incor	Berlin Heart EXCOR
PediaFlow	MEDOS HIA VAD
Micromed DeBakey VAD Child/ Heart Assist 5	Abiomed Biventricular Support 5000
Levitronix CentriMag Blood Pumping System	Abiomed AB 5000
Infant and Child Size Jarvik 2000 VAD	Thoratec Implantable VAD (IVAD)
Levitronix PediVAS	Penn State PVAD
PediPump	Novacor LVAS
Tandem Heart	Toyobo NCVC LVAS
Toddler VAD	Pediatric Cardiac Assist System pCAS
Pediatric pVAD	Cardio Flow PQ
Abiomed Impella cVAD	
Heart Ware Ventricular Assist Device HVAD	
VentrAssist	
Dura Heart	

Tiny Pump	
Circulite Micro VAD	
Levacor VAD	
CorAide	

Table 3 Continuous Flow and Pulsatile Flow VADs

5.5 The Surgical Complications:

Implantation of most types of VADs requires the use of Cardiopulmonary Bypass (CPB) in order to insert the cannulae or grafts inside the heart, including cross clamping the aorta in some cases. Using these techniques has some adverse effects on the patient's heart such as bleeding, infection, neurological complications, thromboembolic events, or renal dysfunction (12). More important is that children in general and neonates in special are more prone to anticoagulation and infection complications, due to their weakness of the immune system, which leads to a higher degree of risk associated with VAD implantation.

The contact between the artificial surface of the VAD and patient's blood activates the coagulation cascade, therefore anticoagulants are required to reduce thrombus formation. On the other hand, using high doses of anticoagulants can cause dangerous bleeding events. Therefore anticoagulation therapy should be controlled very strictly and used as the minimum requirements. Neurological complications and renal dysfunctions are also caused by the unsuccessful management of anticoagulation therapy after VAD implantation. Both are major causes of morbidity and mortality during VAD supports (37).

Infection is the most critical problem facing patients with VAD support. Some MCSDs require the chest to be left open, while other implantable solutions just require one exit point for the percutaneous cable. In both situations there are different possibilities for infection events, depending on the degree on the exposure and the sterilization environment surrounding. Postoperative managements and using antibiotics are still the only options available for patients until the totally implantable VAD without any percutaneous cable is available (37).

Right Ventricular Dysfunction (RVD) may also occur in some patients after implanting LVAD, due to the reduced right ventricular afterload. RVD could be noticed in the prebypass period, the surgical team should transfer the patient from LVAD support to BiVAD support (20).

5.6 VAD's Technical Barriers:

5.6.1 Size:

The anatomical space available for VAD implantation in pediatric patients is one of the major challenges. Firstly, this space is very small at time of birth, so the VAD should be a miniature pump that can fit into this small volume. Secondly, this small space is not fixed in size, this infant will start to grow up and the previous miniature pump will not be suitable, and the VAD replacement surgery is associated with high risk of mortality. Therefore a miniature modular system could be the possible solution for pediatric patients.

5.6.2 Power Source:

All implantable pediatric VADs which are available now need power to run the pump, this power is provided by rechargeable batteries connected with the pump through a percutaneous cable. This cable is associated with a high risk of infection, and limits the ability of the patients to move and practice their normal daily activities. The new VAD should be able to receive the power inductively from an external power source and store it in a battery inside the body, or to generate the power from a source inside the patient's body.

5.6.3 Mechanism of Control:

The most advanced generation of VAD's is based on continuous blood flow design, using either axial flow or centrifugal pumps. In both cases blood flow is not measured directly, but is estimated from the operating parameters of the pump, such as the pump speed and pressure drop. The absence of this kind of blood flow monitor will make the control of the pump very complicated, especially when the body requires various amounts of cardiac output due to the various daily activities. The available techniques are expensive and very complicated, and only a few VADs have a flow probe to measure the exact blood flow. Therefore, an easy, cheap and accurate technique is required to monitor the blood flow and to control the pump performance.

5.6.4 Mechanical Failure:

Patients who received VAD as a DT are those that cannot recover nor have transplantation. These patients' hearts are totally dependent on the VAD, and any mechanical failure could be fatal.

5.6.5 Price:

The cost of implanting a pediatric VAD is around $150,000 including the surgery and hospital accommodation. This large sum of money is due to the extra expensive costs in developing and manufacturing pediatric VADs, but also due to the small quantity of pediatric patients compared with the adults. A new novel cheap material could be the possible solution to overcome this problem.

Chapter 6: The Future

6.1 Integrated Power Source for VAD:

All implantable VADs operated with an external power source system placed outside the patient's body, connected with the implantable pump through a small percutaneous cable. This technique has solved some problems but not all of them, with infection remaining the main cause of morbidity and mortality for patients with implantable VADs. The restriction of movement with this type of power system prohibits some activities such as swimming (51). Therefore, there is a need to look for an integrated power source, which either can be totally implanted inside the patient's body such as nuclear power, or can be generated inside the body from the muscles or the metabolic activities.

6.1.1 Muscle Power Source:

Using muscle to generate power is one of the earliest methods used to generate power inside the human body. Several muscles have been studied for this cause; the most appropriate muscle for generating power is the Lastissimus Dorsi (LD). This muscle is moving continuously with breathing, so it is considered as the non stopping muscle. A special device called Muscle Energy Converter (MEC) is connected with the muscle and used to convert the contractile energy of the muscle into hydraulic power. This type of integrated power source VAD is called Muscle Powered Cardiac Assist Device (MCAD). Muscle power was found to be able to produce energy up to 1.37 J, which is enough to run a VAD at a 60 BPM heart rate or below (51) (52). The diaphragm could be also used to generate power during breathing. The flat sheet of

transducers can placed on the diaphragm and its continuous movement could be converted to an electric current that can run the VAD.

6.1.2 Piezoelectric Source:

Piezoelectric crystals are used to convert the mechanical power to an electrical power, or vice versa. This technique is very well known in the medical field especially for ultrasound and physiotherapy. Stress applied on the moving bones can be applied on a piezoelectric crystal to generate electric power; this requires the continuous moving of the bones which is not achieved during sleeping or resting. This source could be used to partially power the VAD (53).

6.1.3 Thermal Gradient Source:

The thermal gradient between the internal body temperature and the surface temperature could be also a possible source for electric power. This power source has been used previously to power a wrist watch. The main problem with this type is that the thermal gradient is not stable, it changes between summer and winter, and it is suitable just for cold countries not for hot countries (53).

6.1.4 Internal Fuel (metabolic) Source:

The main source of energy for all muscles is Glucose, where the body is using this substance to store the energy. This source can be used to generate power by using special sensors inside the body. This will require the patients to be more careful about their diet. More studies are needed to focus on this technique and decide if this source is sufficient to run an implantable blood pump or not.

6.1.5 Nuclear power Source:

Nuclear power is a small, continuous, long lasting, and clean power source. On the other hand, it needs continuous cooling and a thick housing for shielding which make it very heavy and not suitable for portable applications. Some early studies used nuclear power to operate a total artificial heart and failed for the previous reasons. A small, light weight, and self cooled nuclear reactor could be the future option for implantable devices.

6.2 Filament Support Spindle for Intravascular VAD:

A new axial flow pumped is under development at Virginia Commonwealth University, for adolescent patients. This pump is inserted percutaneously and magnetically levitated. The unique design of this new VAD is that it has an outer cage with radially arranged filaments which will protect the patient's blood vessels (54).

6.3 Fetal Perfusion System:

Around 0.8% of children are born with congenital heart disease worldwide, however if these defects are detected and corrected in utero, results could be changed and less children may need correctional surgical procedures (11). Ension Inc. is developing a system that can support the fetal heart, shown in **Figure -50-**. When a congenital heart defect is discovered in a fetus, it could be possible to correct this defect in utero. This system consists of a centrifugal pump and an oxygenator, with a very small priming volume, offering a pulsatile flow and gas exchange (11).

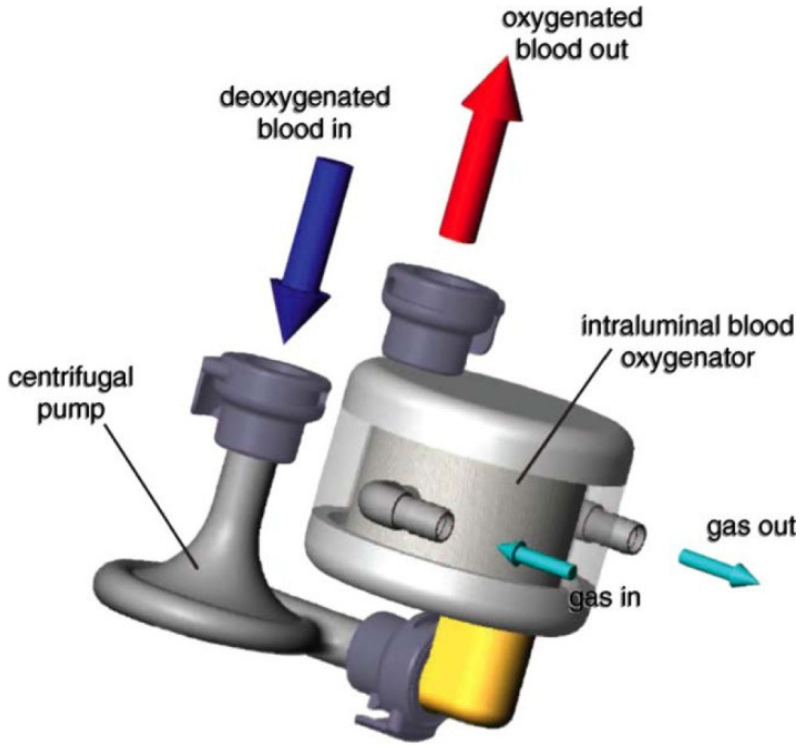

Figure 50 Ension Fetus VAD (11)

Conclusion:

The number of pediatric patients with heart failure is still growing worldwide, and several solutions have been used to help these patients. Medical treatment is not sufficient in many cases, and heart transplantation (HTx) is very limited due to the shortage of donors and not available for all patients at the right time. Therefore, mechanical circulatory support devices have been developed to address this problem; several options have been used such as Extracorporeal Membrane Oxygenation (ECMO), Centrifugal pumps, and Ventricular Assist Devices (VADs).

Although pediatric mechanical circulatory support devices have been widely developed in the last 20 years, the fully implantable pediatric VAD has not been achieved yet. Each of the available pediatric VADs tries to solve one problem, such as the size available for implantation, duration of support, the price, and the intention of therapy as a BTR, BTT, or DT. However, some important issues have not yet been solved such as the integrated power source, pump control mechanism, and the main one is how to overcome the changing of pediatric heart size while he/she is growing. All of these points should be merged together and combined in a VAD that is totally implantable, price affordable, fully powered from an internal source, and is suitable for all pediatric sizes.

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