CHAPTER 9

MECHANICAL CIRCULATORY SUPPORT SYSTEM (MCSS)

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9.1 INTRODUCTION

The heart failure is the only major cardiovascular disease that continues to increase over time, with an estimate prevalence of 1.1-2% both in the United States and in Europe. Furthermore, congestive heart failure is a major health problem with a high mortality rate.

Heart failure is not a specific disease, but a constellation of signs and symptoms arising from different causes: post-hypertensive cardiomyopathy, primary myocardial disease, post-ischemic cardiomyopathy, valvular disease, abnormal ventricular filling and congenital heart disease.

Heart transplantation, as ultimate and effective therapy, is limited by the availability of donor hearts. Since decades researchers have been working to solve this problem by developing Mechanical Circulatory Support Systems (MCSS), that can replace or assist the failing heart. Short-term and intermediate-term ventricular assist devices are used frequently to bridge patients with severe heart failure to recovery.

The early TAHs and VADs were mainly driven from an external pneumatic drive unit. The latest generation TAHs and long-term assist devices are electrically powered, ultracompact, totally implantable, and have small wearable drive/control consoles, allowing patients to return to their daily activities.

The VADs are mechanical blood pumps that can support or replace the function of the failing left ventricle, right ventricle, or both ventricles. The VADs do not require removal of the native heart and therefore can be used as a bridge to transplantation as well as a temporary support system in patients with expected myocardial recovery. DeBakey reported successful LV assist of patients who could not be weaned from the heart-lung machine [1].

The two primary goals of MCSS are to provide adequate perfusion of the vital organs and to decrease cardiac work until the time of heart recovery or heart transplantation. It is often applied in case of acute heart failure after cardiac surgery (postcardiotomy cardiogenic shock), when weaning from extracorporeal circulation is impossible, in cardiogenic shock due to acute myocardial infarction, in acute myocarditis, in acute rejection of transplanted heart or in high-risk patient percutaneous coronary procedures. Other indication can be evolving myocardial infarction: in fact, mechanical unloading of the left ventricle, by reducing energy requirements of the myocardium, can significantly limit the size of infarct [2].

By the supported site, the VADs can be divided into three main groups.

- Left ventricular assist devices (LVADs) blood is withdrawn from either the pulmonary veins, left atrium or the apex of the LV and returned to the ascending aorta. Atrial cannulation is easier to perform and is less traumatic for the heart in comparison to the apical cannulation; it is preferred for a temporary LV support. Left ventricular cannulation via the apex provides a better LV unloading as well as a better VAD performance. For that reason the apical cannulation is preferred for LV assist as a bridge to transplantation.
- Right ventricular assist devices (RVADs): blood is withdrawn from the right atrium and returned to the main pulmonary artery.
- Bi-ventricular assist devices (BiVADs): the BiVADs are actually a combination between LVAD and RVAD, and could be seen as a functional replacement of the heart.

Furthermore, the VADs can be categorised into Intra-Aortic Balloon Pump (IABP), pulsatile and non-pulsatile VADs [3].

The type of ventricular support as well as the device used differs from patient to patient according to the experience and individual preference of the surgical team and

the perspective for ventricular recovery. In current application, for the high severity of the illnesses of target population, there is a general consensus of the scientific panels of minimising ethical conflicts and shifting to rigorous surveillance studies. It is generally underlined the vital role and need of Multicenter Registries [4]. Some of the factors that should be considered in making a decision on which device to use for long-term assistance should include anticoagulation, univentricular vs bi-ventricular failure, mobility, protocol to discharge home and size of patients [5].

Except the IABP, the most frequently implanted devices in Europe are the pneumatic VADs, followed by TAH, centrifugal pumps, and the electromechanical VADs [6].
The main complications during the early phases of mechanical assist are bleeding, right-sided heart failure in case of LVAD, air embolism, progression of multiorgan failure; in the late post-surgical phases the most common complications are infections, thromboembolism and failure of the device [7]. Hemolysis has been observed with centrifugal and axial-flow LVADs [8].

9.2 INTRA-AORTIC BALLOON PUMPING (IABP)

In 1958 Harken at the International College of Cardiology in Brussels describes for the first time a method to treat left ventricular failure by using counterpulsation or diastolic augmentation. He suggests to remove a certain blood volume from the femoral artery during systole and replace this volume rapidly during diastole. By increasing coronary perfusion pressure this manoeuvre would therefore augment cardiac output and unload the functioning heart simultaneously. In 1962 Moulopoulus and co-workers develop a first experimental prototype of intra-aortic balloon (IAB) whose inflation and deflation were synchronised with cardiac cycle [9]. In 1968 IABP enters the clinical practice with a balloon size of 15 French requiring a surgical insertion and a surgical removal. The subsequent introduction of percutaneous insertion (usually through the femoral artery) increased the speed and ease of insertion, thereby providing an impetus for its expanded use in the following clinical settings.

Today continued improvements in IABP technology with smaller balloon size permit safer use and earlier intervention to provide a rapid hemodynamic support in critical, acute conditions of myocardial ischemia and heart failure.

IABP has emerged as the single most effective and widely used circulatory assist device. It is estimated that over 70,000 IABPs are inserted annually in the United States.

After correct placement of the IAB in the descending aorta with its tip at the distal aortic arch (below the origin of the left subclavian artery) the balloon is connected to a drive console. The console itself consists of a pressurised gas reservoir, a monitor for ECG and pressure wave recording, adjustments for inflation/deflation timing, triggering selection switches and battery back-up power sources. The gases used for inflation are either helium or carbon dioxide. The advantage of helium is its lower density and therefore a better rapid diffusion coefficient. Whereas carbon dioxide has an increased solubility in blood and thereby reduces the potential consequences of gas embolisation following a balloon rupture. Inflation and deflation are synchronised to the cardiac cycle. The balloon inflation at the onset of diastole results in both proximal and distal displacement of blood volume in the aorta. Deflation occurs just prior to the onset of systole.

In this way, the IABP has two major hemodynamic effects:

1. blood is displaced to the proximal aorta by inflation during diastole,

2. aortic volume and afterload are reduced during systole through a vacuum effect created by rapid balloon deflation.

These effects may be quite variable, and they depend upon the volume of the balloon, its position in the aorta, heart rate, rhythm, the compliance of the aorta, and systemic resistances [10]. The higher the arterial elastance, which is determined in part by compliance, the greater the hemodynamic improvement from IABP [11]. Despite this variability, expected changes in the hemodynamic profile in the majority of patients with cardiogenic shock include [12]: a decrease in systolic pressure (20%), an increase in diastolic pressure (30%), which may raise coronary blood flow, a reduction of the heart rate (less than 20%), a decrease in the mean pulmonary capillary wedge pressure (20%), an increase in the cardiac output (20%).

To achieve optimal effect of counterpulsation, inflation and deflation need to be correctly timed to the patient's cardiac cycle. This is accomplished by either using the patient's ECG signal, the patient's arterial waveform or an intrinsic pump rate. The most common method of triggering the IAB is from the R wave of the patient's ECG signal. Mainly balloon inflation is set automatically to start in the middle of the T wave and to deflate prior to the ending QRS complex. Tachyarrhythmia, cardiac pacemaker function and poor ECG signals may cause difficulties in obtaining synchronisation: in such cases the arterial waveform for triggering may be used, by identifying the dicrotic notch (aortic valve closure) in the central aortic pressure waveform. If the balloon inflation is too early or the deflation too late the balloon waveform is superimposed to varying degrees over the LV systolic component of the central aortic pressure waveform (i.e. inflation starts when the aortic valve is still open). This results in an increase in afterload, which may result in premature closure of the valve and increase LV work. In this situation, because the incomplete ventricular emptying, the stroke volume and consequently the cardiac output decrease. In addition, a shunt in patients with a septal defect can increase. On the other hand, if the inflation is too late or the deflation is too early, the diastolic augmentation is suboptimal. When the balloon inflation is triggered by pacing spike, this is a potentially lethal mode as loss of capture may result in balloon inflation during systole, as the pump will continue to follow the pacing rate rather than the ventricular contraction rate.

If the patient's cardiac performance improves, weaning from the IABP may begin by gradually decreasing the balloon augmentation ratio (from 1:1 to 1:2 to 1:4 to 1:8) under control of hemodynamic stability. After appropriate observation at 1:8 counterpulsation the balloon pump is removed.

The indications for IABP are cardiogenic shock, treatment of intractable angina, weaning patients from cardiopulmonary bypass, after thrombolysis in patients at high risk for restenosis [13] in high risk or complicated angioplasty, preoperative prophylaxis in patients with severe left main coronary stenosis or critical aortic stenosis.

In a review of 16,909 patients who had an IABP between 1996 and 2000, the most frequent indications for its use were: hemodynamic support during or after cardiac catheterisation (21%), cardiogenic shock (19%), weaning from cardiopulmonary bypass (16%), preoperative therapy in high risk patients (13%), refractory unstable angina (12%), refractory heart failure (6.5%), mechanical complications of myocardial infarction (5.5%), intractable ventricular arrhythmias (1.7%) [14].

The main contraindications for IABP are the presence of severe aortic insufficiency, aortic dissection, prosthetic graft in thoracic aorta, severe peripheral aorto-iliac disease and irreversible brain damage.

The major complications can be related to the vascular district (perforation, ischemia, embolisation and thrombosis), or to the balloon (incorrect positioning, perforation/tear/rupture and gas embolisation).

Female gender, high age and peripheral vascular disease were independent predictors of a serious complication.

9.3 VENTRICULAR ASSIST DEVICE (VAD)

Differently from TAH, the LVAD have a single artificial ventricle connected to the cardiovascular system by maintaining the natural heart. All pulsatile pumps have a flexible blood chamber or a flexible membrane that are compressed and released by air, liquid or by a pusher-plate, thus achieving ejection and filling of blood volume. The presence of input and output valves maintains the unidirectional flow (from the ventricle to the aorta). The driving source can be air (pneumatic system), an incompressible fluid (electro-hydraulically mechanism), a magnet (electromagnetic system) or an electric drive unit (electro-mechanic system). The driving source reaches the pump via a tube trough the skin.

Pulsatile pumps operate in various pump modes: synchronous to the natural heart beat, asynchronous, and a full to empty mode. During the synchronous mode, the pump action is synchronised with the heart action by different operating algorithms and sensors. This allows the device to eject the blood into ascending aorta during the diastolic phase, thus increasing aortic diastolic pressure, and coronary flow. During the asynchronous mode, the device operates in a fixed pump rate.

The console, considered the “brain” of the system, is connected to the blood pump and responsible for controlling the "pumping" action. The blood pumps are the actual "heart" of the systems. Acting in place of the failing heart, they receive blood from the heart and pump it back into the body for circulation to either the lungs or the rest of the body.

Pulsatile pumps show the advantage of maintaining the physiological pulsatility of blood flow with a reduction of both sympathetic drive activity and peripheral vascular resistances, thus improving microcirculation and organ function [15,16]. Furthermore, the pulsatile VADs cause less blood trauma then roller pumps.

The major disadvantage of the pulsatile pumps is the size of components due to the need of a consistent stroke volume blood chamber and required heart valves.

Among these devices, with respect to the implantability degree, there are some external cardiac support systems (Thoratec VAD, Abiomed BVS 5000™, Abiomed AB5000™, Berlin Heart Excor, Medos), other partially implantable (Thoratec HeartMate 1000 XVE, Newcortec BestBeat VAD).

The Thoratec [www.thoratec.com] VAD System, giving circulatory support for either the left side of the heart, the right side, or both sides, includes three major components: blood pump, cannulae, and dual drive console or TLC-II® Portable Driver. The VAD pumps are prosthetic ventricles consisting of a smooth, seamless pumping chamber enclosed in a rigid polysulfone case. The blood sac is manufactured from Thoralon®. Thoralon® has been demonstrated blood and tissue compatibility, thromboresistance, long-term fatigue characteristics and *in vivo* stability.

Two mechanical tilting disc valves maintain unidirectional flow through the blood pump. A sensor detects when the VAD is full of blood and automatically signals the console to eject blood from the pump. In clinical practice, an effective stroke volume of 65 millilitres (ml) is possible with rates ranging from 20 to 110 beats per minute and flow outputs ranging from 1.3 to 7.2 litres/minute (l/min).

FDA approved Thoratec VAD for bridge to cardiac transplantation and postcardiotomy recovery of the natural heart.

Blood flows to the VAD through an atrial or ventricular cannula, and from the VAD with an arterial cannula. All cannulas are manufactured with Thoralon®. Ventricular and arterial cannulas are wire-reinforced to prevent kinking.

The Thoratec Dual Drive Console has two independent and identical drive modules for left and right ventricular support. Each module provides alternating pulses of vacuum and pressure to fill and empty the VAD, thereby providing pulsatile blood flow. In fact, the drive console delivers air to the blood pump in a pulse-like fashion, causing blood to be ejected into the aorta and/or pulmonary artery. Choices of control modes for VAD operation include: asynchronous mode (pumping occurs at a preset rate); volume mode (ejection begins the instant that complete VAD filling occurs); and synchronous mode (pumping is synchronised with the patient's heart rate). The volume mode of operation is used for most patients because of automatic pump response to changes in physiological conditions.

In January 1986, Dr. O.H. Frazier of the Texas Heart Institute (THI) initiated clinical trials for the Thoratec HeartMate IP LVAS (implantable pneumatic), which in 1994 received marketing approval from FDA. Today, the Thoratec HeartMate IP LVAS is used as a bridge to heart transplantation. The pneumatic (air-driven) LVAS is a titanium alloy pump that weighs 570 grams and consists of a blood chamber, an air chamber, a drive-line, and inflow and outflow conduits. Each conduit is a titanium cage that contains a 25-mm porcine valve within a woven Dacron™-fabric graft. With a stroke volume of 83 ml and a maximum pumping rate of 140 beats per minute, the IP LVAS can provide flow rates of up to 12 l/min. The system can operate in automatic mode, fixed-rate mode, and synchronous mode. The drive console can be transported on a wheeled cart, allowing patient mobility.

The HeartMate 1000 XVE (Vented Electric) is similar to the pneumatically driven version, but the pusher plate is driven by a low-speed torque motor instead of air. Percutaneous leads connect the pump to an external console and battery pack. The device can operate either in a fixed-rate mode (50-120 beats/minute) or in an automatic mode. Like the pneumatic variant, the HeartMate 1000 XVE has a maximum stroke volume of 83 ml and it is designed for left ventricular support only. The pump received approval from FDA in 1998.

The ABIOMED BVS 5000™ is used for temporary left, right, or bi-ventricular support in patients with potentially reversible heart failure. The BVS 5000™ underwent preclinical studies at the Texas Heart Institute (THI) from 1986 to 1988 and was introduced for use in patients at THI in 1988. It was the first heart assist device approved by the FDA for the support of heart failure as consequence of cardiac surgery.

This air-driven blood pump is placed outside the body. A unique feature of this system is its dual-chamber design, to provide support for either the left or right ventricle, or both.

The pump houses two polyurethane chambers: an atrial chamber that fills with blood through gravitational force and a ventricular chamber that pumps blood by air-driven power. The atrial chamber is vented outside the patient. The ventricular chamber is connected to the power console by a pneumatic line. Two trileaflet valves separate the atrial and ventricular chambers. The pump can produce blood flow of up to 5 l/min. The BVS 5000™ console can support one or two blood pumps. It is fully automatic and compensates for changes both in preload and afterload; the left and right sides are triggered independently of each other.

The ABIOMED AB5000™ Circulatory Support System can provide left, right, or bi-ventricular support. AB5000™ was introduced for patient use at THI in October 2003.

The pump houses an Angioflex® membrane and two proprietary tri-leaflet valves. The pump, connected to cannulas placed in the heart, fills with blood by gravitational

force and by vacuum assistance from the drive console. The cannulas and drive console are the same as those used for the ABIOMED BVS 5000™. The AB5000™ can provide flow rates of up to 6 l/min. To prevent thrombus formation, systemic anticoagulation is required.

The Newcortec [www.newcortec.com] BestBeat VAD is a new left ventricular assist device, under clinical evaluation in Europe. NewCorTec is an Italian company established in January 2005 to complete the development and industrialisation of an implantable VAD. This VAD had been developed over the previous 10 years with the support of the Italian "Ministry for University and Research".

The BestBeat is a pulsatile, implantable device, with a control algorithm for synchronous counterpulsation with the natural heart and an accessory for both regulating afterload and maintaining synchronous operation. The implantable components of the system are cannulas, pump and percutaneous cable. The implanted pump weights about 500 grams; it has smooth, seamless blood sac and delivers blood from the left ventricle apex to the aorta. The Electronic Control Unit, air filter box and batteries are worn externally. A Control and Monitor Unit (CMU), battery charger and main power supply complete the system. Valved conduits at the pump inlet and outlet maintain forward flow. The blood sac is cyclically compressed and released by a pusher plate moved by an electromechanical actuator; built-in sensors provide control information. The actuator transforms the rotation of an electric motor into a linear motion of the pusher plate (back and forth) by means of a ball screw mechanism.

A particular characteristic is the capability to decrease/increase ventricle workload by varying afterload, always in synchronous counterpulsation, with maximum flow through the pump. This possibility could be extremely important for the gradual weaning patients from the support.

The control algorithm uses signals from internal sensors and flow sensor inside the air filter box for detecting natural heart phase and timing the pump. The system can also operate in fixed rate mode. In synchronous mode, the pump fills during LV systole with a minimum afterload for the natural heart and it ejects during LV diastole maintaining the physiological timing for coronary perfusion.

The Newcortec BestBeat underwent the pre-clinical in vivo tests at the experimental laboratory of the Clinical Physiology Institute (UCCS-Pi S. Piero a Grado, Pisa, Italy), conducted by Tecnobiomedica S.p.A.. The final GLP animal tests were performed at the Institute Mutualiste Montsouris in Paris, France. A multicenter clinical study is ongoing in Europe.

9.4 ROTARY BLOOD PUMP

The roller pumps are similar to the pumps used for cardiopulmonary bypass. The inflow and outflow cannulas are connected by tubing made partially of silicone rubber. The silicone part is placed in a head with rotating occlusive rollers. During the head rotation, the tubing is compressed repeatedly by the rollers and a unidirectional non-pulsatile blood flow is generated. The roller pumps are simple to use and are relatively low cost devices. They are available in every cardiac surgery and the cannulas used are the same as those used for cardiopulmonary bypass. However, the roller pumps have some major disadvantages: requirement of systemic anticoagulation, blood trauma leading to hemolysis, tubing spallation and fatigue, non-pulsatile or low-pulsatility flow. These limitations preclude their use beyond few hours or days [17].

The centrifugal pumps consisted of non-occlusive pump head positioned within rigid pump housing. The rotating head consists of a various number of impeller blades that generate a non-pulsatile unidirectional flow by creating a vortex. Centrifugal pumps do not require artificial valves. The centrifugal pumps, like the roller pumps, are simple to use and inexpensive. In contrast to the roller pumps, the centrifugal pumps are pressure limited, virtually eliminating the potential for air aspiration or tubing disruption. Moreover, the centrifugal pumps are less destructive to blood cellular elements and cause lower hemolysis, when compared with the roller pumps [18].

As a consequence, the centrifugal pumps have replaced roller pumps in 30% of routine cardiac surgery procedures, especially for procedures that are more prolonged [18]. The centrifugal pumps are currently used for a short-term mechanical cardiac assist. However, experimental studies demonstrated that some centrifugal pumps could be used for longer period [19].

The major disadvantage of the centrifugal pumps is the non-pulsatile flow, and the relatively low pressure difference that can be bridged.

The Hemopump® (Medtronic, Inc., Minneapolis, MN, USA) is a catheter-mounted transarterial transvalvular LVAD that can be used for short-term LV support. The device, described in 1988 by Wampler et al. [20], works on the principle of the Archimedes screw, rotating at up to 25,000 (revolutions·min^{-1}). The impeller, integrated into the aspiration cannula, is activated by a flexible cable connected to an external high-speed electromotor. The tip of the cannula is positioned into the left ventricle via the femoral artery or via the ascending aorta. Blood is withdrawn from the LV and discharged into the descending aorta, providing non-pulsatile flow. Initially, the Hemopump® generates a continuous nonpulsatile flow. In a poorly contracting or non-contracting ventricle, the nonpulsatile flow persists. As ventricular function recovers and stroke volume increases, the aortic valve opens and a pulsatile flow returns.

The Hemopump® has been available in different variants: a 14 French version for percutaneous insertion, a 21 French version for introduction via graft anastomosed to the femoral artery, and a 31 or 26 French version (Sternotomy Hemopump®) for direct introduction into the ascending aorta. The 14-French variant is designed for LV support during high-risk PTCA and allows flows up to 1.5 l/min. The 21-French variant allows flows up to 3.5 l/min. The sternotomy variant (31-26-French) allows flows up to 5-4.5 l/min. The last variant is useful in patients who cannot be weaned from cardiopulmonary bypass or in patients with severe peripheral vascular disease.

Hemopump® is indicated as a short-term LV support of patients in cardiogenic shock after open-heart surgery and for performing coronary artery bypass graft operation on the beating heart without cardiopulmonary bypass. The device was used in the past as a LV support in patients undergoing high-risk coronary angioplasty as well. Contraindications for Hemopump® implantation include the presence of an artificial aortic valve as well as the presence of thrombi in the LV.

The Hemopump® combines the direct LV unloading, typical for LVAD, with the fast and simple transarterial implantation of the IABP. In contrast to IABP, the Hemopump® is not synchronised with the patients ECG and therefore works properly even during severe arrhythmia or cardiac fibrillation. Many physicians are concerned about the possibility of severe hemolysis during the Hemopump® assist. The level of plasma free haemoglobin indeed increases during the initial period of assistance, but within the first 24 hrs decreases and stabilises near normal [21].

Like the IABP, the percutaneous implantation of the Hemopump® could be problematic in patients with severe peripheral arteriosclerosis or kinking, especially if a larger cannula is used. The major complications during the assist are related to mechanical pump failure, such as fracture of the drive cable and expulsion of the

cannula out of the ventricle [22, 23]. The Hemopump®, if not running, can induce substantial regurgitation through the pump into the left ventricle.

Although still used clinically in Europe, the Hemopump® is not longer in production and is not currently available in the United States [24].

The Impella® [www.abiomed.com] devices are catheters with microaxial flow pump that can support the heart with up to 5.5 litres of blood per minute. The catheters can be implanted percutaneously, via a cut-down, or in the operating room. In Europe, the Impella® circulatory support systems received CE Mark approval. Impella® recover has been designed for low output patients. Ventricular Unloading Catheters can be used for left or right ventricle recovery. The sizes of catheters vary from 24-34 French (surgical direct application trough right atrium or pulmonary artery to right ventricle, up to 6 l/min), 21 F (directly via ascending aorta to left ventricle, or peripherally trough femoral artery, up to5 l/min), to 12 French (percutaneous access, femoral artery, up to 2.5 l/min). They can be applied for 5-7 days.

9.5 INTRA-AORTIC BALLOON PUMPING (IABP), VENTRICULAR ASSIST DEVICE (VAD) AND HEMOPUMP NUMERICAL MODELS

In CARDIOSIM© software different mechanical circulatory support system (MCSS) as intra-aortic balloon pumping (IABP), ventricular assist device (VAD) producing pulsatile flow and rotary blood pump (Hemopump) producing continuous flow, were implemented.

Intra-aortic balloon pumping (IABP) model According to Jaron [25, 26], the IABP model, inserted in the arterial tree, is considered as a flow source $Q_{IABP}(t)$ (Figure 9.5.1) in the following way: during the diastole the balloon inflates and the flow is positive, and during the next systole the balloon deflates and the flow is negative (Figure 9.5.2).

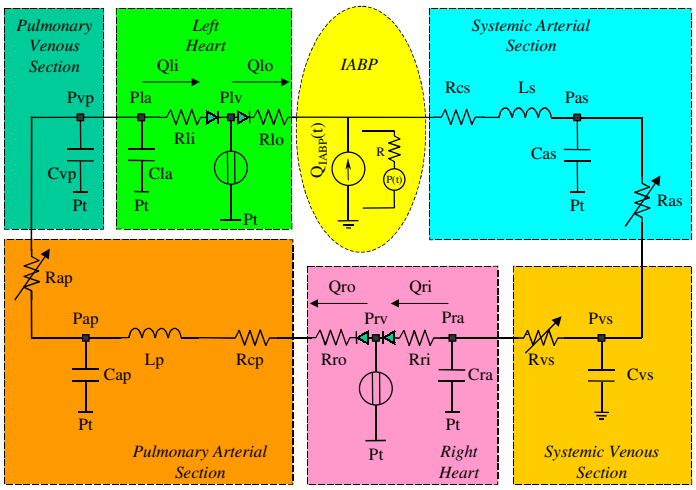

Figure 9.5.1 The structure of the basic cardiocirculatory network when the IABP is inserted.

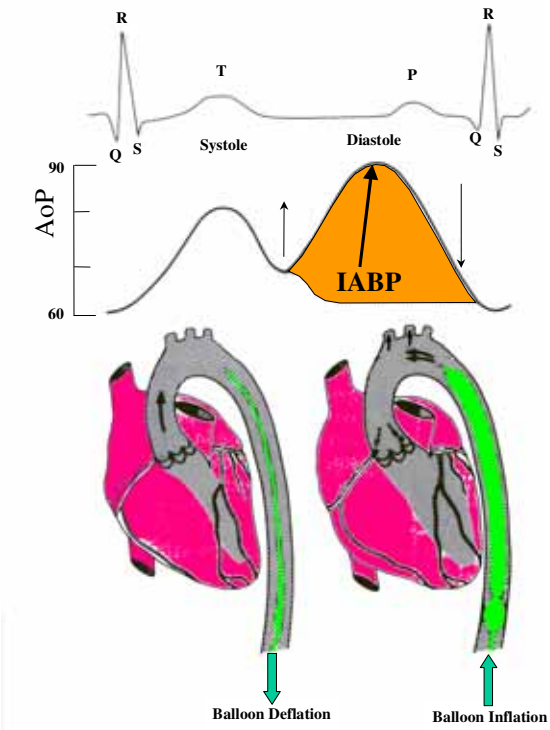

Figure 9.5.2 Intra-aortic balloon pumping temporization: during the systole the balloon deflates and during the next diastole the balloon inflates. AoP is the aortic pressure.

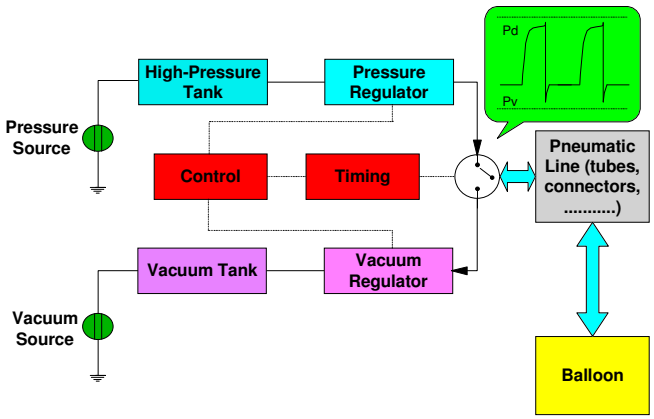

Figure 9.5.3 General layout of the driving unit of the IABP system. The waveform reported in the call-out represents the air pressure waveform in the balloon. Pd and Pv are the driving and vacuum pressures respectively.

The flow source [$Q_{IABP}(t)$] may be replaced by a pneumatic pressure source [P(t)], representing the compressed gas reservoir, and by resistance (R) representing the total gas delivery resistance of the system. The pneumatic source [P(t)] has been modelled by describing separately the ejection and the filling as the air outflow from a high-pressure tank, connected to the pressure source, and the air outflow from a lower-pressure tank connected to the vacuum source [27, 28].

The driving gas of the assist device was assumed to be ideal. A simplified description of the physical phenomenon underlying the filling and ejection phases of the balloon is sufficient for this purpose.

Figure 9.5.3 shows the general layout of the driving unit of the balloon system.

In the model of IABP the following values can be adjusted: driving positive pressure (Pd), vacuum pressure (Pv), balloon volume and timing. The intra-aortic balloon pumping must be synchronised with the ECG.

Figure 9.5.4 represents the output produced by the CARDIOSIM© software when the intra-aortic balloon pumping assistance was applied. Figure 9.5.1 shows the cardiovascular network used to produce the graphical output.

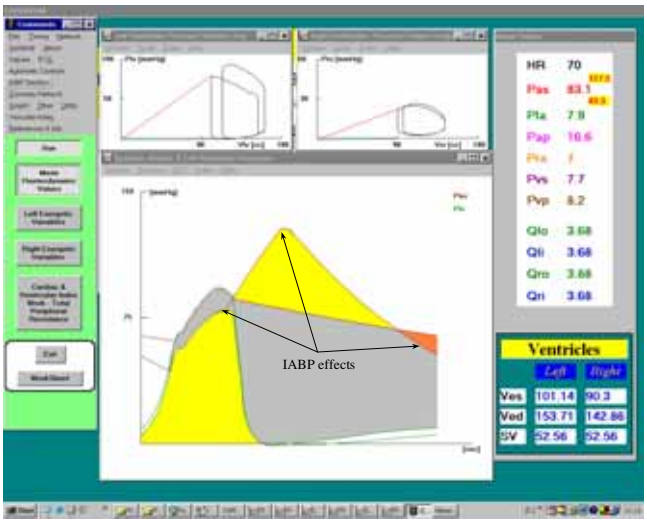

Figure 9.5.4 Graphical output produced by the CARDIOSIM© software when the IABP assistance was applied. The cardiovascular network was assembled using the schema reported in Figure 9.100. Middle window shows the left ventricular (Plv) and systemic arterial (Pas) pressures waveforms before and after the IBAB activation. In the right window were presented the mean pressure and flow values obtained when the IABP was applied.

The yellow and orange area (middle window in Figure 9.5.4) under the systemic arterial pressure (Pas) waveform reassume the effects of IABP assistance. The most significant contribution of the IABP are mainly due to its effects on preload (left upper window in Figure 9.5.4), afterload and aortic pressure (hemodynamic effects). The most significant contribution of the IABP, however, is on the myocardial oxygen supply and on coronary blood flow. Analysing Figure 9.5.4 it is possible to observe that the IABP

substantially increases the peak of aortic pressure and decreases end-diastolic aortic pressure. Simultaneously, there is a decrease in systolic ventricular pressure and systolic arterial pressure.

Ventricular assist device (VAD) model In CARDIOSIM© software a pneumatic artificial ventricle model, used to simulate the effects of the ventricular assist device (VAD) application, was implemented. The representation of the ventricle is achieved by considering separately filling and ejection phases. Figure 9.5.5 (panel a) shows the general layout of the driving unit-pneumatic ventricle system. The ejection is described by the air outflow from a high-pressure tank connected to a pressure source towards a lower pressure tank, which is the ventricle itself. Filling is achieved by the air outflow from a higher-pressure tank (the ventricle itself) to a lower-pressure tank connected to a vacuum source. This is a simplified description of the physical phenomenon underlying the filling and ejection phases in the ventricle.

The basic assumption adopted [27, 28] are the following:

- Air pressure waveform in the artificial ventricle is determined by the interaction between air mass flow generator and a compliance (the membrane of the ventricle – Figure 9.5.5 panel b).
- The gas changes characteristic, assumed to be adiabatic and of the first order near the working point.

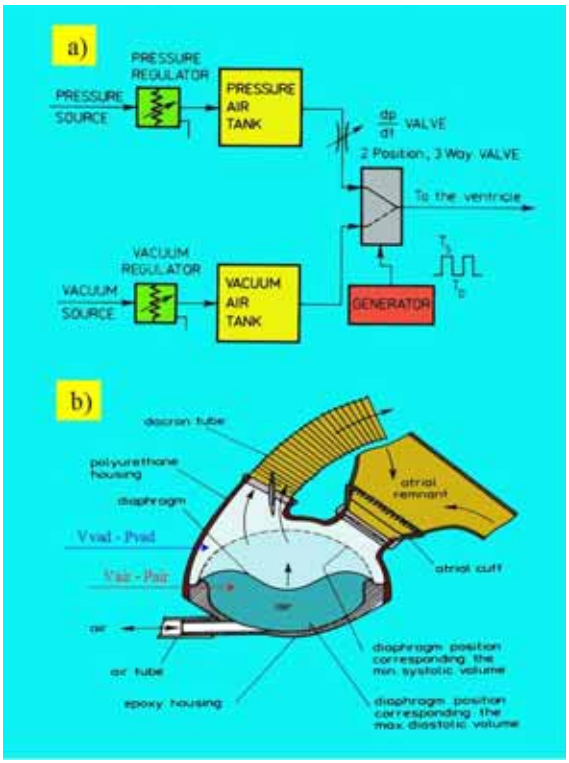

Figure 9.5.5 Panel a) shows the general layout of the driving unit-pneumatic ventricle system. Ts and Td represent the systole and diastole time respectively. Panel b) illustrates the pneumatic ventricle. Dashed and continuous lines inside the ventricle represent two different position of the membrane. Vair and Pair (Vvad and Pvad) are the volume and the pressure into the part of the ventricle connected to the air tube (into the ventricle).

With these assumptions the equation employed is the following:

$$F = S \cdot Pi \sqrt{\frac{2 \cdot g}{R \cdot T}} \cdot \sqrt{\frac{m}{m-1}\left[\left(\frac{Pe}{Pi}\right)^{2/m} - \left(\frac{Pe}{Pi}\right)^{(m+1)/m}\right]} \tag{9.5.1}$$

where F is the mean air flow, S is the flow section, Pi is the absolute pressure of the gas in the outflow tank, Pe is the absolute pressure of the gas in the inflow tank, m is the adiabatic exponent, R is the gas constant, T is the absolute temperature of the gas and g is the gravity acceleration.

A diaphragm represents the interaction between the air and the liquid in the pneumatic ventricle with the characteristic shown in Figure 9.5.6. It is assumed that the pressure drop across the diaphragm is far from minimum (Vmin) and maximum (Vmax) values and, outside these limits, it is increasing with the compliance of the diaphragm, which may be different in end-systolic and end-diastolic positions.

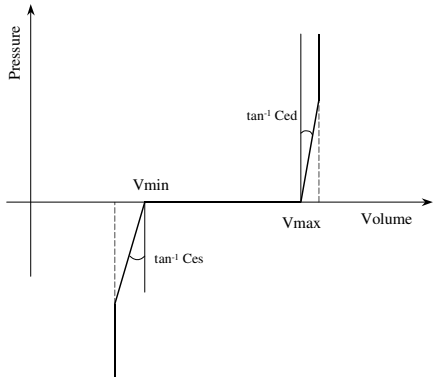

Figure 9.5.6 Pressure-volume relationship which has been assumed for the pneumatic ventricle diaphragm in its end-systolic and end-diastolic positions. Ced and Ces are respectively the diaphragm compliance at end-diastolic and end systolic positions. Vmin and Vmax are respectively the minimum and the maximum pneumatic ventricular volume.

Two constants in the final equations (9.5.2 and 9.5.3) take into account the characteristics of the tube connecting the ventricle to the pressure and vacuum tanks and the characteristics of the pneumatic circuit.

Equation 9.5.1 is valid for $Pe \geq 0.536Pi$: this condition is usually verified in the pneumatic ventricle. The generator described by equation 9.5.1 interacts with a compliance, which can be assumed to be the slope of the tangent to the gas characteristic around the working point.

Considering these conditions it is possible to write the following equation for the filling [28]:

$$\dot{Pair} = \frac{1}{Vair^{-6}} \cdot \left[Kd \cdot Pair \cdot \sqrt{E1 \cdot \left[\left(\frac{Pv}{Pair}\right)^{E2} - \left(\frac{Pv}{Pair}\right)^{E3}\right]} - Pair^{-6} \cdot \dot{Vair} \right] \tag{9.5.2}$$

and for the ejection phase:

$$\dot{Pair} = \frac{1}{Vair^{-6}} \cdot \left[Ks \cdot Pd \cdot \sqrt{E1 \cdot \left[\left(\frac{Pair}{Pd} \right)^{E2} - \left(\frac{Pair}{Pd} \right)^{E3} \right]} - Pair^{-6} \cdot \dot{Vair} \right] \qquad (9.5.3)$$

where $E1=[m/(m-1)]$, $E2=(2/m)$ and $E3=[(m+1)/m]$. Kd and Ks are two constants. $Vair=(Vt + Vmax - Vvad)$, Vt is the air tube volume and Pd (Pv) is the driving (vacuum) pressure.

In the presented model, the variables affecting the pneumatic ventricular performance which can be modified are (in addition to the compliances and constants): driving pressure and vacuum pressure, pneumatic ventricular frequency (HR) and its systole-to-diastole ratio (SD).

The same model is employed in the simulation of the left (and/or right) ventricular assist device using different control algorithms (delayed, variable and fixed stroke volume (SV)). Figure 9.5.7 illustrates as the pneumatic ventricle is connected to the cardiocirculatory network.

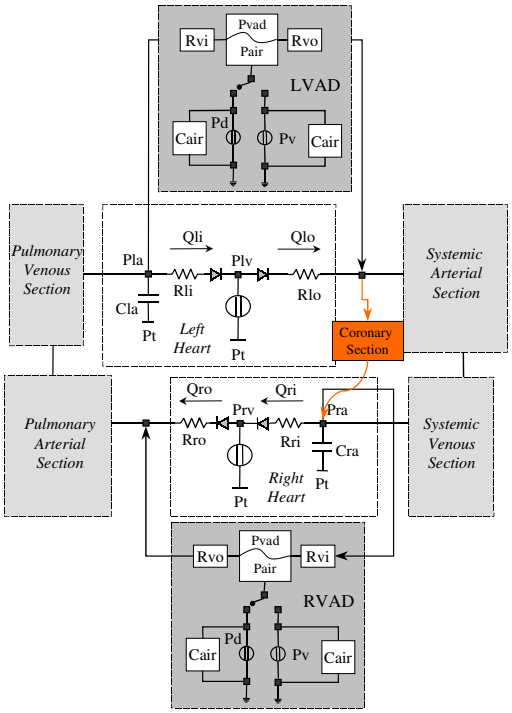

Figure 9.5.7 Pneumatic ventricle connected as left (right) ventricular assist device LVAD (RVAD). Bi-ventricular assist device (BVAD) is realised when LVAD and RVAD are simultaneously activated.

When pneumatic ventricle is connected as left ventricular assist device (LVAD), the assistance takes blood from the left atrium and ejects blood in aorta (parallel connection). It is possible to realize a serial connection when the assistance takes blood form the left ventricle.

When pneumatic ventricle is connected as right ventricular assist device (RVAD) the assistance takes blood from the right atrium and ejects it in pulmonary artery (parallel connection). If the assistance takes blood from the right ventricle it is possible to realize a serial connection.

In CARDIOSIM© software different configurations (less or more complex) can be choose to simulate systemic (pulmonary) arterial section and coronary circulation.

Figure 9.5.8 shows a graphical output produced by CARDIOSIM© software when pathological condition was reproduced and LVAD was applied to assist the left ventricle. In this figure it is possible to see the left (left upper window) and right (right

upper window) ventricular loops in pathological (cycle A) and assisted (cycle B) conditions. In the middle large window the left ventricular and systemic arterial pressures in pathological (waveforms A) and assisted (waveforms B) conditions are represented. The left column shows: the heart rate, the mean pressures in the cardiac cycle, the mean flow, for both ventricles the end-systolic, end-diastolic volumes and the stroke volumes. The values presented are referred to the assisted condition.

Finally in the central panel the end-systolic, end-diastolic volumes, the stroke volume and the flow produced by the LVAD are reported.

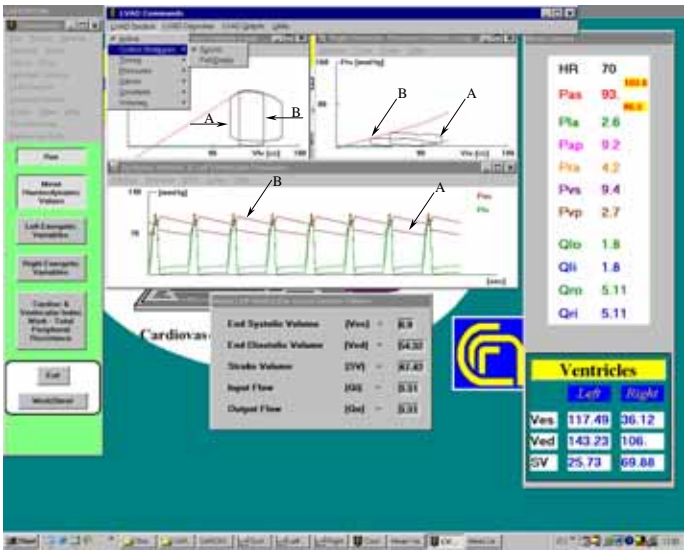

Figure 9.5.8 Output produced by CARDIOSIM© software when LVAD was applied. During the experiment the assistance was synchronised with the natural heart and was set a delay of 200 msec (respect to the ventricular systole). In the assisted condition the total flow was 5.11 l/min and was produced in part by the left natural ventricle (1.8 l/min) and in part by the LVAD (3.31 l/min).

Axial-flow pump (Hemopump®) model Among the devices used for heart recovery, an important role is played by non-pulsatile devices as their characteristics make their use rather simple and competitive in comparison to other devices such as intraaortic balloon pump (IABP).

Hemopump® HP31 device (Medtronic, Inc., Minneapolis, Minnesota, USA) is among them: it is a miniature rotary blood pump introduced into the left ventricular cavity through the aortic valve. This ventricular assist device (VAD) uses cannula inserted through the aortic valve to aspirate the blood from the left ventricular cavity and to eject it into the ascending aorta.

The capability to be inserted into the circulatory system without major surgery makes the pump almost as safe and convenient as the IABP. This pump may be more effective than IABP in assisting failing left ventricle [29]. In contrast to IABP, this kind of ventricular assist device is not synchronized with the patient's ECG and therefore works properly even during arrhythmia or cardiac fibrillation. In this study, according with

Bai's works [30, 31], we modeled Hemopump® type HP31. This VAD can be operated at seven different rotational speeds ranging from 17000 to 26000 rpm, with an increment of 1500 rpm [32].

The direct effects of the Hemopump® on the hemodynamic variables of the circulatory system includes an increase in mean aortic pressure, in total cardiac output (left ventricular output flow plus Hemopump® flow), a decrease in the area of the pressure-volume loop of the left ventricle with consequent decrease in blood flow pumped out by the ventricle [33, 34]. In addition, the pump produces a decrease in left atrial pressure [29]. The increase in mean aortic blood pressure increases the coronary blood flow, which in turn increases the oxygen supply to the heart. Even if what is considered here is a specific device, most of these considerations can be extended to any of the existing devices of the same type.

Figure 9.5.9 shows the Hemopump® electric analogue. The pump model is connected to the circulation model in such a way that it aspirates blood from inside the ventricular model (QHin) and expels the blood into the arterial section (QHout). In the model represented in Figure 9.5.9 [30, 31] R is a resistance and L is an inertance. Qn is a constant flow source: its value depends on the rotational speed of the pump. L represents the effects of the inertial properties of the blood in the pump.

Changing the resistance (R) value (and Qn value) it is possible to simulate seven different rotational speeds [30, 31] from 17000 to 26000 revolutions·min^{-1} with a step of 1500 revolutions·min^{-1}.

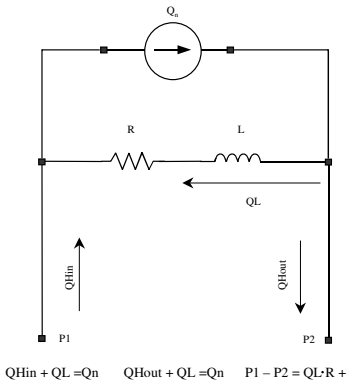

Figure 9.5.9 Electric analogue of Hemopump® HP31 assist device.

In CARDIOSIM© simulator the Hemopump® device was connected to the cardiovascular system as a left ventricular assist device (Figure 9.5.10).

In this figure the left and right heart (described in Chapter 2) and the systemic and thoracic circulation (described in Chapter 3) are illustrated.

The coronary section was implemented using the complex coronary circulation model illustrated in Chapter 3 (Figure 3.5.3). The pulmonary circulation was implemented using the model showed in Figure 3.4.1.

The Hemopump® assist device connected as LVAD aspirates the blood from the left ventricle and ejects it in the systemic artery.

When present, Pt represents the mean intrathoracic pressure.

All the equation of the model (Figure 9.5.10) are presented in Appendix 9.I.

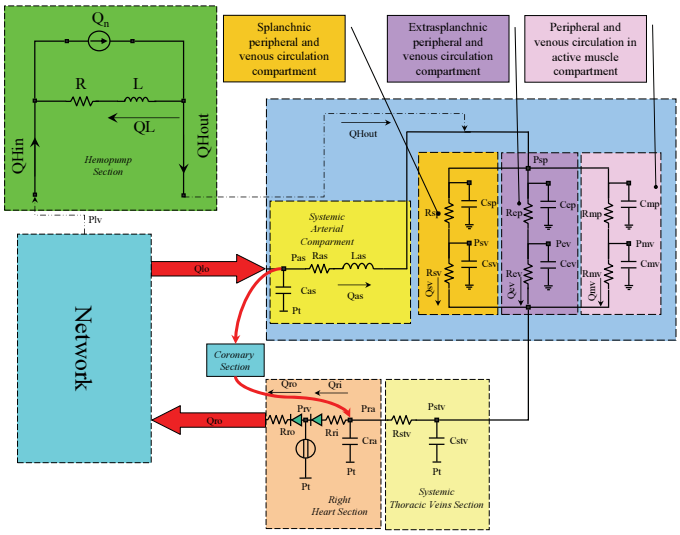

Figure 9.5.10 Electric analog of the cardiovascular system and Hemopump® assist device connected as LVAD. Pas, Psp, Psv, Pev, and Pmv are respectively the systemic arterial, splanchnic peripheral, splanchnic venous, extrasplanchnic venous and venous in active muscle compartment pressures. Qas is the systemic arterial flow. Qsv (Qev) is the splanchnic (extrasplanchnic) venous flow. Qmv is the venous flow in the active muscle compartment. QHout (QHin) is the output (input) pump flow.

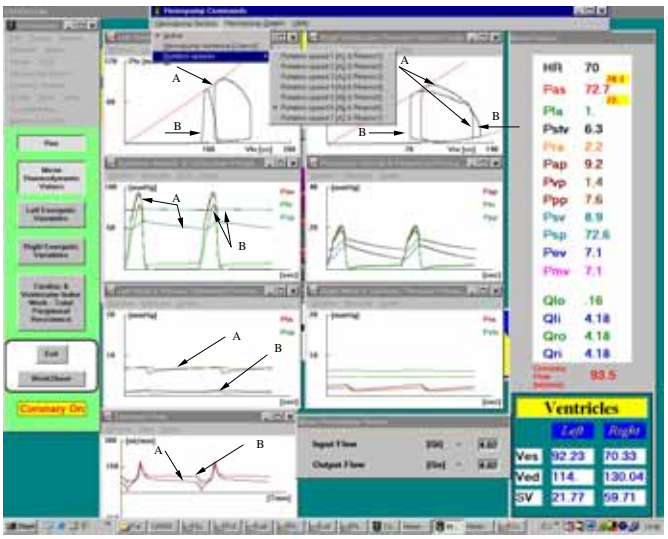

Figure 9.5.11 Graphical output produced by CARDIOSIM© software when Hemopump® was applied. Labels A (B) were referred to a pathological (assisted) condition. The flow produced by assistance was of 4.02 l/min at a rotational speed of 24500 revolutions·min^{-1}.

Figure 9.5.11 presents an output produced by CARDIOSIM© software when the LVAD was applied. The mean values presented on the right column were referred to the assisted condition. The waveforms with label A (B) were obtained during the pathological (assisted) condition. The rotational pump speed was of 24500 revolutions·min^{-1} and produced a flow of 4.04 l/min. The consequence of Hemopump® action on left ventricular volumes (left upper window – Figure 9.5.11) consists of a reduction (cardiac cycle B) of end-diastolic volume (Ved) and of end-systolic volume (Ves). In the right ventricle (right upper window) it is possible to observe a reduction of the end-systolic volume and an increase of the end-diastolic volume. The total flow was of 4.18 l/min and only a small part of it was produced by the natural heart.

Finally the LVAD application produced an increase in the coronary blood flow (left lower window).

Appendix 9.I

The equations for the left (right) atrium, systemic arterial section, splanchnic (extrasplanchnic) peripheral and venous circulation, peripheral and venous circulation in active muscle compartment, systemic thoracic veins and pulmonary arterial, peripheral and venous sections are the following (Figures 3.5.3 and 9.5.10):

$$Qlo = \frac{Plv - Pas}{Rlo}$$

$$Qlo = \dot{Pas} \cdot Cas + Qas + Qa1$$

$$(Pas + Pt) - Psp = Qas \cdot Ras + \dot{Qas} \cdot Las$$

$$Qli = \frac{Pla - Plv}{Rli}$$

$$Qri = \frac{\mathrm{Pr}\, a - \mathrm{Pr}\, v}{Rri}$$

$$Qri + \dot{\mathrm{Pr}}\, a \cdot Cra = \frac{Pstv - \mathrm{Pr}\, a}{Rstv} + Qv1$$

$$\mathrm{Pr}\, v - Pap = Qro \cdot Rro$$

$$\frac{Pstv - \mathrm{Pr}\, a}{Rstv} = \dot{Pvs} \cdot Cvs + Qsv + Qev + Qmv$$

$$Qep = Qev + \dot{Pev} \cdot Cev$$

$$Qmp = Qmv + \dot{Pmv} \cdot Cmv$$

$$Qas + QHout = (Qsp + \dot{Psp} \cdot Csp) + (Qep + \dot{Psp} \cdot Cep) + (Qmp + \dot{Psp} \cdot Cmp)$$

$$Qro = \frac{\mathrm{Pr}\, v - Pap}{Rro}$$

$$Qsv = \frac{Psv - (Pstv + Pt)}{Rsv}$$

$$Qev = \frac{Pev - (Pstv + Pt)}{\mathrm{Re}\, v}$$

$$Qmv = \frac{Pmv - (Pstv + Pt)}{Rmv}$$

$$Qsp = \frac{Psp - Psv}{Rsp}$$

$$Qep = \frac{Psp - Pev}{\mathrm{Re}\, p}$$

$$Qmp = \frac{Psp - Pmv}{Rmv}$$

The equations for the pulmonary compartment (Figure 3.4.1) are:

$$\dot{Qap} \cdot Lap = Pap - Ppp - Qap \cdot Rap$$

$$\dot{Pap} \cdot Cap = Qro - Qap \qquad Qvp = \frac{Pvp - Pla}{Rvp} \qquad Qpp = \frac{Ppp - Pvp}{Rpp}$$

$$\dot{P}pp \cdot Cpp = Qap - Qpp \qquad \dot{P}la \cdot Cla + Qli = Qvp \qquad \dot{V}lv = Qli - (Qlo + QHin) \qquad \dot{V}rv = Qri - Qro$$

$$\dot{P}vp \cdot Cvp = Qpp - Qvp$$

Vlv (Vrv) is the left (right) ventricle volume.

$$Psv = \frac{1}{Csv} \cdot [V_{TOT} - Cas \cdot (Pas + Pt) - (Csp + Cep + Cmp) \cdot Psp - Cev \cdot Pev$$
$$- Cmv \cdot Pmv - Cra \cdot (\Pr a + Pt) - Cap \cdot (Pap + Pt) - Cpp \cdot (Ppp + Pt)$$
$$- Cpv \cdot (Ppv + Pt) - Cla \cdot (Pla + Pt) - Cstv \cdot (Pstv + Pt) - Vrv - Vlv - Vu]$$

$$Vu = VuAS + VuSP + VuEP + VuSV + VuEV + VuRA +$$
$$VuAP + VuPP + VuPV + VuLA + VuAMP + VuAMV + VuSTV$$

V_{TOT} is the total blood volume (5300 ml), $VuLA$ ($VuRA$) is the left (right) atrium unstressed volume, $VuAS$ ($VuAP$) is the systemic (pulmonary) arterial unstressed volume, $VuSP$ ($VuSV$) is the splanchnic peripheral (venous) unstressed volume, $VuEP$ ($VuEV$) is the extrasplanchnic peripheral (venous) unstressed volume, $VuAMP$ ($VuAMV$) is the active muscle peripheral (venous) unstressed volume, $VuPP$ ($VuPV$) is the pulmonary peripheral (venous) unstressed volume and $VuSTV$ is the systemic thoracic venous unstressed volume.

The equations for the coronary section (Figure 3.5.3) are the following:

$$Qa1 = \frac{(Pas + Pt) - Pca}{Ra1}$$

$$Qa1 = \dot{P}ca \cdot Ca + Qa2$$

$$Qa2 = \frac{Pca - (Pcc + LVP)}{Ra2}$$

$$Qa2 = Qv2 + \dot{P}cc \cdot Cc$$

$$Qv2 = \frac{(Pcc + LVP) - Pcv}{Rv2}$$

$$Qv2 = Qv1 + \dot{P}cv \cdot Cv$$

$$Qv1 = \frac{Pcv - (\Pr a + Pt)}{Rv1}$$

LVP is the isovolumic pressure generator.
The equations for the Hemopump® numerical model are the following:

$$QHin + QL = Qn \qquad QHout + QL = Qn \qquad Pas - Plv = QL \cdot R + \dot{Q}L \cdot L$$

References

1. DeBakey ME. Left ventricular bypass pump for cardiac assistance. Clinical experience. *Am. J. Cardiol.* 1971; 27: 3-11.
2. Meyns B, Stolinski J, Leunens V, Verbeken E, and Flameng W. Left ventricular support by Catheter-Mounted axial flow pump reduces infarct size. *JACC* 2003; 41(7): 1087-1095.
3. Mihaylov D, Verkerke GJ, Rakhorst G. Mechanical Circulatory Support Systems, a review. *Technology and Health Care* 2000; 8 (5): 251-266.
4. Stevenson LW, Kormos RL. Mechanical Cardiac Support 2000: Current Applications and Future Trial Design. *JACC* 2001; 37: 340-370.
5. Arabia FA, Smith RG, Rose DS, Arzouman DA, Sethi GK, Copeland JG. Success rates of long-term circulatory assist devices used currently for bridge to heart transplantation. *ASAIO J* 1996; 42: M42-M46.
6. Quaini E, Pavie A, Chieco S, Mambrito B. The Concerted Action 'Heart' European registry on clinical application of mechanical circulatory support systems: bridge to transplant. The Registry Scientific Committee. *Eur. J. Cardiothorac. Surg.* 1997; 11: 182-188.
7. Goldstein DJ, Oz MC, Rose EA. Implantable Left Ventricular Assist Devices. *NEJM*, 1998; 339: 1522-1533.
8. Nakazawa T, Machinouchi K, Takami Y, Glueck J, Takatani S, Nose Y. The effect of the impeller-driver magnetic coupling distance on hemolysis in a compact centrifugal pump. *Artif Organs* 1996; 20: 252-257.
9. Moulopoulos SD, Topaz S, Kolff WJ. Diastolic balloon pumping (with carbon dioxide) in the aorta - a mechanical assistance to the failing circulation. *Am Heart J* 1962; 63: 669.
10. Weber KT, Janicki JS. Intraaortic balloon counterpulsation. A review of physiological principles, clinical results, and device safety. *Ann Thorac Surg* 1974; 17: 602.
11. Marchionni N, Fumagalli S, Baldereschi G, Di Bari M, Fantini F. Effective arterial elastance and the hemodynamic effects of intraaortic balloon counterpulsation in patients with coronary heart disease. *Am Heart J* 1998; 135 (5 Pt 1): 855-61.
12. Scheidt S, Wilner G, Mueller H, et al. Intraaortic balloon counterpulsation in cardiogenic shock. *N Engl J Med* 1973; 288: 979.
13. Ohman EM, Califf RM, George BS, Quigley PJ, Kereiakes DJ, Harrelson-Woodlief L, Candela RJ, Flanagan C, Stack RS, Topol EJ. The use of intraaortic balloon pumping as an adjunct to reperfusion therapy in acute myocardial infarction. The Thrombolysis and Angioplasty in Myocardial Infarction (TAMI) Study Group. *Am Heart J* 1991; 121 (3 Pt 1): 895-901.
14. Ferguson JJ, Cohen M, Freedman RJ, Stone GW, Miller MF, Joseph DL, Ohman EM . The current practice of intra-aortic balloon counterpulsation: results from the Benchmark Registry. *JACC* 2001; 38:1456-62.
15. Anstadt MP, Tedder M, Hegde SS, Perez TR, Crain BJ, Khian HV, Abdel AS, White WD, Lowe JE. Pulsatile versus nonpulsatile reperfusion improves cerebral blood flow after cardiac arrest. *Ann Thorac Surg* 1993; 56: 453-461.
16. Fukae K, Tominaga R, Tokunaga S, Kawachi Y, Imaizumi T, Yasui H. The effects of pulsatile and nonpulsatile systemic perfusion on renal sympathetic nerve activity in anesthetized dogs. *J Thorac. Cardiovasc. Surg.* 1996; 111: 478-484.
17. Richenbacher WE, Pierce WS. Assisted Circulation and the Mechanical Heart.In: Braunwald E, ed. Heart Disease: a Textbook of Cardiovascular Medicine; pp534-547. Philadelphia: W.B. Saunders Company, 1997.

18. Golding LAR, Smith WA. Centrifugal Pumps - Now and Future. In: Ungar F, ed. Assisted Circulation. Berlin: *Springer* 1995; 142-151.
19. Olsen DB. Rotary blood pumps: a new horizon [editorial]. *Artif. Organs* 1999; 23: 695-696.
20. Wampler RK, Moise JC, Frazier OH, Olsen DB. In vivo evaluation of a peripheral vascular access axial flow blood pump. *ASAIO Trans* 1988; 34: 450-454.
21. Wampler RK, Frazier OH, Lansing AM, Smalling RW, Nicklas JM, Phillips SJ, Guyton RA, Golding LA. Treatment of cardiogenic shock with the Hemopump left ventricular assist device. *Ann. Thorac. Surg.* 1991; 52: 506-513.
22. Baldwin RT, Radovancevic B, Duncan JM, Wampler RK, Frazier OH. Management of Patients Supported on the Hemopump® Cardiac Assist System. *Texas Heart Institute Journal* 1992; 19: 81-86.
23. Wiebalck AC, Wouters PF, Waldenberger FR, Akpinar B, Lauwers PM, Demeyere RH, Sergeant PT, Daenen WJ, Flameng WJ. Left ventricular assist with an axial flow pump (Hemopump): clinical application. *Ann. Thorac. Surg.* 1993; 55: 1141-1146.
24. Sweeney MS. The Hemopump in 1997: a clinical, political, and marketing evolution. Ann Thorac Surg 1999; 68:761-763.
25. Jaron D, Moore TW, He P. Theoretical considerations regarding the optimisation of cardiac assistance by Intra-aortic balloon pumping. I*EEE Trans. On Biomed.* Engineering 1983; 30: 177-186.
26. Jaron D, Moore TW, He P. Control of Intraaortic balloon pumping: theory and guidelines for clinical applications. *Annals of Biomedical Engineering* 1985; 13: 155-175.
27. Ferrari G, De Lazzari C, Mimmo R, Tosti G, Ambrosi D. A modular numerical model of the cardiovascular system for studying and training in the field of cardiovascular physiopathology. *Jour. Biomed. Eng*. 1992; 14: 91-107.
28. Guerrisi M, Ferrari G, Arabia M, Mimmo R, Szurmak Z. Investigation on cardiac function of a pneumatically driver artificial ventricle. *Biocib. Biomed. Eng*. 1987; 7: 103-120.
29. Meyns B, Nishimura Y, Racz R, Jashari R, Flameng W. Organ perfusion with hemopump device assistance with and without intraaortic balloon pump. *The J. Of Thoracic and Cardiovascular Surgery*. 1997; 114(2): 243..
30. Bai J, Bing Z. Simulation evaluation of cardiac assist device. *Methods of Information in Medicine.* 2000; 39: 191.
31. Li X, Bai J, He P. Simulation study of the Hemopump as a cardiac assist device. *Medical & Biological Engineering & Computing*. 2002; 40: 344.
32. Meyns B, Siess T, Laycock S, Reul H, Rau G, Flameng W. The heart-Hemopump interaction: A study of the Hemopump flow as a function of cardiac activity. *Artificial Organs*. 1996; 20: 641.
33. Waldenberger FR, Wouters P, Deruyter E, Flameng W. Mechanical unloading with a miniature axial flow pump (Hemopump): an experimental study. *Artificial Organs*. 1995; 19: 742.
34. Marks JD, Pantalos GM, Long JW, Kinoshita M, Everett SD, Olsen DB. Myocardial mechanics, energetics, and hemodynamics during intraaortic balloon and transvalvular axial flow Hemopump support with a bovine model of ischemic cardiac dysfunction. *ASAIO J.* 1999; 45(6): 602.