State of the Art Mock Circulation Loop and a Proposed Novel Design

T. Batuhan Baturalp and A. Ertas
Department of Mechanical Engineering, Texas Tech University, Lubbock, TX, USA

Abstract — A novel fully-automated systemic mock human circulation loop (MCL) design is proposed with a wide literature review of MCL and left ventricular (LV) form and function. Drawbacks and strengths of current MCLs and their pumping systems are investigated and an inference has been made for requirements of a novel MCL design. It has been found that proposed MCL design should not only capable of replicating wide range of cardiac operating scenarios, but also pumping system should better represent LV for simulating various cardiovascular diseases particularly muscular dysfunctions. Also, the proposed MCL design should be fully-automated that controls essential MCL parameters such as compliance, resistance. Medical papers showed that LV has principal functionalities such as elastance, torsional and twisting motion of ventricular wall, which play important role on motion and contraction of LV. These features are implemented on a proposed pneumatic muscle actuated LV.

Keywords: MCL, Mock circulation loops, Mock circulatory systems, Pneumatic Mock Left Ventricle

1 Introduction

Heart disease is agreed as the highest cause of death in the world by most of the health organizations. Heart disease and stroke statistics of American Heart Association [1] states that, on basis of 2009 death rate data, cardiovascular disease was the reason for one of every three deaths in the United States. According to other sources, 2150 Americans die because of cardiovascular disease each day which is an average of one death every 40 seconds. Heart failure can be treated by medications, medical devices and surgery. With respect to another source [2], approximately 4000 cases each year require a heart transplant, however only less than half of them can receive one. Currently, there are about 5 million Americans who suffer because of heart failure, and over 500,000 patients are diagnosing each year [3]. The increasing donor shortage and limited heart transplant waiting time generates a need for a temporary solution such as an assistive device to keep the patient alive while a donor is being found. Most of the cardiac failures happen in the left side of the heart which is the part of the heart that pumps blood to the body. Left Ventricular Assistive Devices (LVADs) have been developed to increase the cardiac flow output of the LV chamber.

While LVADs provide a solution for patients who suffer from cardiac insufficiency, Valvular Heart Disease (VHD) is widely accepted as another significant portion of heart diseases. Valvular heart disease involves problems on one or more of the valves of the heart (the aortic and mitral valves on the left and the pulmonary and tricuspid valves on the right). It can be treated by medication and generally with valve repair or artificial heart valve replacement. In 2003, over 290,000 heart valve operations were performed worldwide with an increase of 10 to 12% per year. Thus, a rough estimation can be made that it will exceed 850,000 in 2050 [4]. Another study [5] shows that VHD covers a percentage between 10% and 20% of all cardiac surgical procedures in the United States. Up to the present, over 4 million people across the world have received an Artificial Heart Valve (AHV) [6]. Replacement of artificial heart valves have been done in last six decades, since the first replacement performed in 1952. During the last six decades more than 50 artificial heart valves have been designed developed [7].

MCLs play an essential role not only in vitro testing (not in a body) and development of LVADs and AHVs, but also other circulation related devices such as total artificial hearts, artificial lungs, vascular grafts, bioreactors for tissue engineered heart valves and intra-aortic balloon pumps. Cardiac device design procedures generally adopt MCLs before advancing to animal or clinical trials which are much more troublesome and expensive. With respect to standards of The American Society for Artificial Internal Organs (ASAOI) and the Society of Thoracic Surgeons (STS), experimental flow loops should correctly represent significant parameters of the human circulatory system under normal and worst-case physiologic conditions [8]. Also, Clemente et al. [9] published an article which conducts the setup of technical standard for mechanical heart assist devices and approach to problems related to technical standards for biomedical devices. Various physiological cardiac failure or operating scenarios needs to be replicated in the MCL for testing, including but not limited to LVADs and heart pumps. These different scenarios require a fully-automated MCL which can reproduce the necessary conditions precisely and switch between them without trouble. Based on listed essential MCL functionalities, not only MCL actuator parameters such as geometry, different movement trajectories and elastance of ventricular wall, but also versatility of the MCL parameters such as resistance and compliance are critical and needed to be developed for imitating different scenarios of human circulation on an experimental setup.

The aim of this study is to propose a novel MCL design which is fully automated, and capable of replicating wide range of cardiac operating and failure scenarios including
mimicking the movements of left ventricular chamber of heart. The novel design of a new MCL should include some several important factors. A wide literature review is presented in this paper to seek these factors on MCLs. These factors can be listed as versatility of the hemodynamic parameters like resistance and compliance. In addition, the pump of the MCL should be more realistic than the ones in the literature, since the state of art pulsatile blood pumps are not capable to mimic torsion and wringing action of the LV, muscular dysfunctions of the heart and more realistic shape of the chamber.

1.1 Background

Mock circulatory loops in the literature, can be categorized into two main groups with respect to their flow types: non-pulsatile and pulsatile systems. Generally, flow type is defined by the pump or actuator of MCL. Non-pulsatile flow MCLs uses continuous pumps such as centrifugal or axial pumps, while pulsatile MCLs are equipped with various pumps (piston, cam driven, diaphragm based pumps, and pneumatically and hydraulically operated pressure chambers) in the literature. Recent developments showed that normal physiological cardiac conditions can be reproduced by using slaughterhouse pig hearts which are used for their morphological and physiological similarities to human hearts.

The initial MCLs were mainly used on testing artificial hearts. One of the earliest MCL was built by Kolff et al. [10] in 1959. It was including both systemic and pulmonary circulation loops, and the ventriciles were activated by use of compressed air chambers. The biggest incomplete side of this design was resistance, because no resistance valve is used in this study. Another early in vitro test setup was developed by Bjork et al. [11] in 1962 to examine prosthetic mitral and aortic valves. The study claims that developed system was capable of accurately simulate various physiological conditions. The system consisted of interconnected valve testing chambers, aortic analogue, peripheral resistance, and left atrium analogue. Peripheral resistance and vertical position of the reservoir were adjustable. Main contribution of this study was usage of collapsible molded rubber sac LV. A good example for initial MCL designs with flexible tubing and cam driven ventricle was Reul et al.’s [12] design in 1974. Their study was also one of the leading studies that used Windkessel chamber with adjustable air volume for compliance. The downside of this study was lacking of suitable connection to connect VADs. Pennsylvania State University mock circulation system is another example to remarkable MCL designs which is developed by Rosenberg et al. [13] in 1981. The MCL consisted of resistance, compliance, inertia, systemic and pulmonary circulation, VAD connections, and adjustable cardiac conditions. While the MCL represented acceptable results and provided a proper in vitro testing setup for artificial hearts, inertia values were incorrectly assumed to be equal for systemic and pulmonary circulations.

As stated previously, MCL can be categorized into two main groups as pulsatile and non-pulsatile with respect to their flow generation types. Since there are many studies in the literature about MCLs, this categorization can be widened regarding to type of mock circulation system’s pumps. Many different pumping and actuation systems are used on MCLs but they can be categorized into four principal groups such as: biological, piston, VAD, and pressure chamber based pump systems.

1.1.1 MCLs with Biological Pump Systems

In recent years, biological pumps systems were started to use in MCLs in order to create more realistic simulations. In most of the studies in the literature, entire explanted hearts were integrated into in vitro setups. The reason behind this approach is allowing a better preservation of the anatomical structures and at the same time not including all the physiological complexities of animal models. Other advantages of using explanted hearts are, enabling the potential applications of new experimental apparatus, or surgical procedures since the environment is more familiar to surgeons to operate and analyze their hemodynamic effects.

Since the use of entire explanted hearts is inconvenient due to the required protocols, complexity and cost, it had been suggested by Richards et al. [14] to use the explanted hearts as a passive structure which means pressurizing the blood from another source and using the chamber feature of the heart. An external pulsatile pump was used in this study, and results were found to be not optimal especially in terms of flow rates and the pressure wave forms. This study was followed by Leopaldi et al. [15] by using an entire explanted porcine heart, whose LV is pressurized by an external pumping system. Electrically conditioned latissimus dorsi muscles are also used for actuation in various studies [17 - 20].

Most of the whole heart mock loop designs were accomplished to maintain cardiac contractility ex-vivo. The explanted working-heart models were capable of reproducing the physiological ventricle pressure-volume relationship with state of art mimicking the shape and motion of the real heart, although the complexity and costs of the related experimental protocols represented serious drawbacks. The PhysioHeart platform was developed by Hart et al. [20] to overcome some gaps in the study of comprehensive cardiac mechanics, hemodynamics, and device interaction of MCLs. Cardiac performance of the MCL was controlled and kept at normal levels of hemodynamic performance for up to four hours. Cardiac changes and performance of an entire heart during an explantation into the developed in vitro apparatus are investigated by Chinchoy et al. [21]. Similarly, left ventricular ejection function of ex resuscitated pig hearts was examined by Rosenstrach et al. [22]. Left ventricular function was restored and maintained in all six hearts for 30 min in this circuit. Although usage of explanted whole hearts has great advantages such as reproducing the ventricular wall motion,
geometry, and contraction, they have a major drawback on duration of experimentation since they don’t contract more than six hours. This drawback makes fatigue and long-term testing of cardiovascular devices impossible which are crucial on validation of these devices.

1.1.2 MCLs with VAD Pumps

VADs are used in MCLs not only as a testing device, but also as the main or driving pump. Naturally, those pumps are already tested and usually already available in the market. In this section, brief information will be given about MCLs that use ventricular assistive devices as the main pump.

One of the pioneer studies that utilize a VAD as the major pump of the MCL is researched by Schima et al. [23] who sought for simple and inexpensive solutions for common problems of MCLs. Another study that measures the performance of artificial blood pumps by using them as pump in a MCL is conducted by Knierbein et al. [24]. Also LVADs were used to simulate left ventricular function and aortic flow by Papaioannou et al. [25].

1.1.3 MCLs with Piston Pumps

Piston pumps are advantageous with their mechanical simplicity, reliability, and ease measurement of the variables of interest such as ventricular pressure and volume. They are also more controllable compared to other pumps. Downside of the piston pumps can be pointed as hard to mimic the pulsatile flow and elastic nature of the heart and always has to be in a cylindrical shape which is not similar to real left ventricular shape. In this section, MCLs from selected papers in the literature which are equipped with piston pump as the main pump of the loop will be introduced.

In vitro reproduction of the LV and arterial tree in a mock circulatory system and interaction of them with a left ventricular assist device was examined by Ferrari et al. [26]. In another study of Ferrari et al. [27], an elastance model is used to mimic the Frank Starling’s law for reproducing more realistic hemodynamic values. Singh et al. [28] developed a pulsatile MCL in order to test robustness of artificial heart valves and their effects on the parameters associated with the circulatory system. In LVAD studies, not only the design of the device is important but also the control of the device is essential. On this purpose, Vaes et al. [29] was designed and developed a MCL which was capable of featuring the properties of the (diseased) heart and mimicking the baroflex response of the heart.

1.1.4 MCLs with Pressurized Chambers

The need for better elastance, ventricular shape, pulsatile flow and simulating the Frank Starling law led the authors surface the idea of using pressurized chambers for representing the ventricles of the heart. Both pneumatic and hydraulic pressurized chambers were used in the literature. In this section, a brief survey on MCLs that uses pressurized chambers as heart ventricles will be introduced.

A systemic MCL was established to investigate the movements of the heart valves during pulses of the heart by Verdonck et al. [30]. In this study, atria and LV were represented by an elastic bag made of latex in a hydraulic type (water) chamber. Pantalos et al. [31] developed a MCL which was equipped with a pneumatic chamber and flexing polymer sac for testing VADs under normal, heart failure, and partial recovery test conditions. Another pneumatic pressurized chamber type driven systemic MCL was built by Patel et al. [32] to validate LVADs under congestive heart failure, exercise and normal conditions. Arrhythmias and diastolic function problems were focused by Mouret et al. [33] who has constructed a new systemic MCL that was driven by the dual activation simulator. Pantalos et al. [34] developed a mock circulation that behaves differently under altered physiologic conditions for testing cardiac devices. The purpose of the study was to assess the ability of the mock ventricle to mimic the Frank Starling response of normal, heart failure, and cardiac recovery conditions. As seen in the literature of pressurized chamber pump type MCLs, versatility for creating operating conditions and replicating ventricular geometry shines out among features of MCLs. On the other hand, there is still room for development on features like mimicking ventricular wall motion, contraction, and muscle fiber orientation and also operating conditions like muscle dysfunctions which is one of the most common cardiovascular diseases.

2 Novel Design of MCL

A wide literature review has been conducted on MCL designs to investigate the needs to be improved on a novel MCL design. First of all, capability of mock LVs needs to be improved for replicating human LV chamber’s movements and physiological parameters for different scenarios such as healthy-rest, healthy-exercise, various cardiovascular diseases and failure states. Additionally, a fully-automated and controllable circulation system is needed in the literature since controllable MCLs has been started to introduce to literature, recently. One example to this kind of studies was conducted by Legendre et al. [35] which was equipped with an engine like mechanism pump system that simulates the LV. Pump system uses a piston to push a diaphragm which enables to create an unsteady flow. Normal healthy and pathologic state patient conditions were simulated in the tests, and their results were compared to results in the literature. The system was found as accurate to simulate in vivo conditions. By current technological developments on the sensors and data acquisition systems, a fully automated and controllable MCL can be built that utilizes controllable valves for resistance, controlled air pressurized compliance chambers for compliance (also known as the reciprocal of elastance) and inertiance can be controlled by the geometry of the tubes and properties of system fluid which has reasonably stable value in human circulation. These parameters will be adjusted to
simulate different cardiovascular states in addition to pump of the system. The pump of the system should be more realistic than the ones in the literature, since the pulsatile blood pumps are not capable to mimic torsion action of the LV, muscular dysfunctions of the heart and more realistic shape of the chamber. An in vitro beating heart simulator should be developed which has seen in the literature as needed for reducing the required time to develop, test, and refine of cardiovascular instruments such as heart valves and assistive devices in general.

Ideal pulsatile pump of a MCL was defined by Knierbein et al. [24] that it should be capable to replicate dynamic properties of the physiological load as close as possible for generating physiological flows and pressures at the intersection between pump and mock loop. Resistances and volumes must be variable in a range which for different pump sizes and different circulatory conditions approximates physiological conditions. Handling of the system must be simple and reliable in order to facilitate reproducibility of test parameters.

The fully-automated systemic MCL was designed in Computer Aided Design (CAD) environment which can be seen in Figure 1.

![Figure 1 Developed MCL with Annotations.](image)

The developed MCL consists of two compliance chambers for systemic and aortic compliance values. The left ventricular simulator, pressure and flow sensors, resistance valves, a drain container for resetting the system, signal conditioner for the flow sensor, a data acquisition device to digitize outputs of the sensors, and atrial chamber as open air container with adjustable height to generate constant pressure are the other components of developed MCL. Clear tygon tubing with different diameters were used in the system and integrated to the CAD environment with respect to bending radius of the selected tubing. A steel cart was used to add mobility to the design. A bypass tubing from bottom of the left ventricular simulator to aorta was made for mounting the LVADs to the system. This bypass tubing was considered and designed as optional by adding a valve to the bottom of the left ventricular simulator. A pressure sensor was also added to the output of the left ventricular assistive device to evaluate its performance. Clamp-on tubing type flow meters were investigated in the literature for ease of use and non-invasive features to the system, since no physical contact is required with the fluid media. Only one ultrasonic flow sensor (Transonic, ME20PXL) was selected because it is easy to relocate the flow sensor for obtaining measurements from different locations. A stand for left ventricular simulator was also designed to support it while not constraining its contractive motion. Another function of this stand was holding the artificial heart valves and making easier assemble/disassemble process to test different types of heart valves.

Measurement of pressure from various locations in a MCL is essential. Main locations to measure pressure in a systemic MCL are upstream and downstream of the compliance chambers, outlets of atrium and left ventricular chamber and ventricular assistive device. Since compliance chambers are designed with air pressure based adjustment, air pressure transducers are also required.

Human circulatory system has two main resistances which are the systemic and pulmonary. The developing MCL has only systemic circulation and resistances in the sections of MCLs are dependent on the length and cross-sectional area of the pipe. Thus, proportional control valve to adjust level of systemic resistance is crucial in mock circulatory loop design. A computer-controlled proportional valve (Hass Manufacturing Company, Model EPV-375B) was chosen which operates between 1-5 V DC control signal and this valve represents the total peripheral resistance of the circulatory system.

When the blood pressure in a blood vessel increases, it reacts with expanding its volume. This characteristic of the blood vessels is called compliance. It can be considered as inverse of the stiffness since compliance value increases with increasing flexibility. Therefore, compliance should be considered as a controlled parameter in a fully-automated MCL. On this purpose, two pressurized air type compliance chamber were included which represents compliance of pulmonary artery and aorta. These compliance chambers were equipped with computer controlled air regulator to enable the automation of MCL.

### 2.1 Pump Design of MCL

Developing a realistic mock left ventricular chamber that mimics shape and wall movements of a real LV requires a wide investigation on not only shape and motion of LV, but also orientation and contraction of myocardial fibres. The transformation of the heart shape during the beating is found to be directly related to the pumping performance of the heart. Thus, the motion of the LV wall is essential on replication of the pumping function of the LV. In this section, some studies about left ventricular shape, motion, myocardial fiber orientation and torsion will be introduced and a prototyped pneumatic left ventricular pump will be demonstrated.
Left ventricular form and geometry and impact on its function and efficiency investigated by Buckberg et al. [36] and Sengupta et al. [37]. The effect of myocardial fiber orientation on contractility and helical ventricular myocardial band concept are revealed by Torrent-Guasp [38]. Helical ventricular myocardial band concept was an innovative new concept for understanding three dimensional, global, and functional structure of the ventricular myocardium. Another important aspect for wall motion of LV is the twisting movement of the ventricle during systole which was investigated in detail first time by Streeter et al. [39]. Accepted opinion [40, 41] on cause of the torsional movement of the LV is possible due to the helical orientation of myocardial fibres and the promising opinion on function is creation of a suction effect to assist the diastolic filling. Additionally, the systolic twisting motion stores energy which is to be used during diastole for ventricular filling [42].

In the context of gathered information about architecture of LV, a pneumatic muscle actuated mock LV prototype was manufactured. The geometry was created by lofting cross-sectional representations of left ventricular chamber and it was inverted in CAD environment to obtain mold geometry. The mold consists of three different parts as seen in Figure 2 and it was prototyped by using a 3D printer. While two components of the mold were used to create the outer layer of the LV, the part in the middle creates the inner layer.

The printed mold was filled with “Dragon Skin” brand high performance silicone which is reasonably strong and elastic. Additionally, a second mold was designed for forming one solid band in which the custom pneumatic muscles were placed in the desired formation. After the pneumatic muscle band is created by placing three pneumatic muscle fibers together (Figure 3), the band is inserted into the main mold in a helical formation as seen in Figure 4 which shows the completed LV chamber. The pneumatic muscle strips are connected to a series of pressure regulators that contract the ventricle to produce the same effect as that of a real left ventricle. The custom made pneumatic muscles are made from rubber tubing and black pneumatic mesh. While one end of the muscle was folded over and sealed, an inflation needle was inserted at the other end.

The result of the initial tests showed that silicon tissue structurally strong enough since no tears or rips were seen. On the other hand, silicon LV did not deform enough due to high thickness of the LV wall. Contraction was found to be insufficient because of air leaks on custom made pneumatic muscles and thickness of the tissue. However the proof of concept is considered as successful since mock LV wall motion resembles the real LV wall motion. Sufficient contraction can be reached by improvements on thickness of the tissue and performance of pneumatic muscles.

3 Conclusions

Design of a novel fully-automated systemic MCL was proposed in this paper. A wide review on current MCLs and physiological features of LV was conducted and presented. In the light of literature review findings, computer controlled MCL design which is capable of replicating various cardiac operating conditions and able to switch between them smoothly was proposed. Additionally, geometry and wall motion of the real LV was attempted to be implemented on actuator of proposed MCL by prototyping a pneumatically actuated mock LV. The prototyped LV was found to be insufficient in terms of contraction but the reasons of insufficiency were found and improvements are on the way.

4 References


[23] Schima, H., H. Baumgartner, F. Spitaler, P. Kuhn, and E. Wolner. “A modular mock circulation for hydromechanical studies on valves, stenoses, vascular grafts and cardiac assist


