A Complete Mock Circulation Loop for the Evaluation of Left, Right, and Biventricular Assist Devices

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Abstract: A new mock circulation loop was developed to replicate the necessary features of the systemic and pulmonic circulatory systems, including pulsatile left and right ventricles coupled with vascular compliances and resistances. A brief description of the mock loop construction is provided before results are presented confirming the recreation of perfusion rates and pressures found in the natural systemic and pulmonic vascular trees for a normal and failing heart at rest. This rig provides the ability to evaluate the hemodynamic effect of left, right, and biventricular assist devices in vitro. The small and compact mock circulation rig has the potential to reduce device evaluation costs by simulating the natural circulatory system, thus providing valuable device performance feedback prior to expensive in vivo animal trials. Key Words: Pulsatile mock circulation loop—Ventricular assist device—Hemodynamics.

A mock circulation loop is an essential in vitro tool for cardiovascular device design evaluation. Although a mock circulation loop does not replace in vivo trials, a design may be efficiently refined beforehand by ascertaining its effect on circulation hemodynamics. This accelerates the design process and is necessary to comply with Food and Drug Administration regulations before expensive animal and human trials (1).

Ventricular assist device (VAD) programs incorporate mock circulation loops to test design iterations. Current mock circulatory loops can be generally classified as either simple and nonpulsatile in nature or advanced, including parameters to imitate the physiology of the natural human circulatory system.

Many VAD programs use a simple loop as the quickest and most efficient means of testing a newly designed pump’s ability to meet natural physiological requirements (2–4). Although introducing blood into these loops allows for the assessment of hemolysis and thrombosis (5), the effect on pump performance when inserted into the intended pulsatile system cannot be assessed.

Therefore, various centers have created pulsatile mock circulation loops to simulate systemic circulation in order to evaluate left VADs (6–9). However, these systems are not sufficient to assess bi-VADs, which require the additional simulation of the pulmonic circulation. Furthermore, the effect of LVAD insertion on right-heart function and pulmonary circulation cannot be comprehensively evaluated.

The techniques of pulse replication in these systems do not always rely on passive ventricular filling during diastole, thus limiting the Frank-Starling (10,11) response to changing physiological conditions. For example, these systems often employ a diaphragm sac that relies on negative pressure around the sac to induce flow into the ventricle.

Recent mock loops have attempted to improve performance and suitability. Pantalos et al. (12) successfully developed an artificial ventricle that adheres to the Frank-Starling law; however, it is limited to a systemic loop only. Wu et al. (13) identified the need for pulmonary and systemic loop simulation to test the response of physiological feedback controllers.

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One of the first mock vasculatures, the Donovan loop, attempts to recreate systemic and pulmonic circulation parameters and is used to evaluate total artificial heart designs (14). Consequently, the rig does not incorporate an artificial ventricle and is therefore not suitable for evaluating the performance of assist devices. However, it may be adapted to further advance basic mock circulation loops. As such, the Donovan loop is now regularly used by research centers for VAD testing (15–17).

A systemic and pulmonary mock loop should adhere to the Frank-Starling law, which is characterized by a change in ventricular function in response to variations in preload. Additionally, the mock circulatory system should have the ability to alter its hemodynamic characteristics to emulate varying degrees of left and/or right-heart function (normal, enhanced, failing) under several physiological conditions (rest, exercise). Finally, there should be provision to easily introduce mechanical assistance.

Therefore, the purpose of this article is to describe the design and construction of a new complete mock circulation loop (Fig. 1) and to demonstrate the ability to simulate normal and heart-failure conditions. The evaluation of VAD insertion on this reproduced cardiovascular system is achieved by Timms et al. (18).

METHODS

Complete mock loop design

Successful development of a circulation loop that closely simulates the natural cardiovascular system requires a comprehensive knowledge of cardiovascular anatomy and hemodynamics. Techniques are then required to create an analog of this anatomy, generate control parameters to influence the hemodynamics, and measure performance.

The presented rig follows the Frank-Starling response to all simulated physiological conditions by design and features reproducible and independently variable levels of left or right-heart function. Easily variable vascular parameters are included to dictate natural hemodynamic values. The rig simulates the autoregulatory mechanisms of the cardiovascular system in response to changing heart condition and simulated drug therapy. Most importantly, however, systemic and pulmonary circulation loops are connected in series. Figure 2 details the circulation path and rig components. Mechanical assist devices may be inserted into the loop by plumbing the inlet of the pump into the ventricle and the outlet into the corresponding artery.

The complete mock circulation system was constructed as a loop containing heart and vascular components of the systemic and pulmonary circulations. The components were assigned functional parameters obtained from the natural cardiovascular system to reproduce expected hemodynamic characteristics for each physiological condition.

Heart

Natural heart simulation was achieved by constructing a complete left and right mock heart composed of passive atrial and pneumatically actuated ventricular chambers.

Structure

The open-to-atmosphere atria were constructed from 40-mm clear PVC piping to replicate atrial compliance. This enabled the atrial chambers to change
fluid volume in response to venous return, and hence pressure head was directly proportional to this fluid level. The ratio of volume change to pressure head defines this value of compliance. A sufficient atrial/ventricular pressure gradient was produced to passively fill each ventricle during the diastolic phase.

Rapid ventricular filling occurred through 40-mm diameter mitral/tricuspid brass swing check valves. These valves possess sufficiently low forward resistance to flow while preventing fluid backflow during ventricular systole. The ventricular chambers are similar in construction to the atrial chambers, with the addition of an end cap that was tapped with a hose tailpiece to allow compressed air to be input during systole and vented during diastole.

Function

The rate of ventricular contractions is controlled with a dSPACE controller board (DS1104, Novi, MI, U.S.A.) and CONTROLDESK software. These contractions are simulated by incorporating a 3/2 solenoid valve (SMC-317, Indianapolis, IN, U.S.A.) in the air driveline for each ventricle. Signaling the solenoid “on” allows the compressed air into the chamber (systole) while signaling the solenoid “off” vents the developed air pressure within the ventricle (diastole). The switching rate determines the heart rate, while the percentage time “on” and “off” during each cycle influences the systolic and diastolic times, and consequently, the air volume input into the ventricle.

A specified driveline mass flow rate of air is created from a pressure-regulated air compressor source and input into the ventricular chamber above the water level during systolic periods. This action ejects fluid through the aortic/pulmonary check valve. The fluid level just before this period is dependent on the ventricular preload/atrial pressure and represents the end diastolic volume (EDV).

Contractility is automatically altered by changes in preload/EDV. For example, an increase in EDV as a result of increased preload reduces the amount of air above the fluid in the chamber prior to systole. This increases the rate of pressure rise (contractility) in the ventricle for a set mass flow rate and is the guiding principle embodied in the Frank-Starling law.

Contractility can be further varied by altering this driveline air mass flow rate by the actuation of additional regulators situated at the inflow to each ventricle. These regulators set a maximum ventricular pressure and therefore allow the desired physiological condition to be set. This has advantages over an animal model, because left or right-heart failure is repeatable and can be independently induced. Values for left and right-heart functionality are displayed in Table 1 for conditions of normal rest and left heart failure (LHF). A constant heart rate of 60 bpm was simulated for each condition, with a systolic period of 40%. Higher simulated heart rates are possible to reproduce exercise conditions; however, the maximum perfusion rate is limited by the minimum inherent resistance of the pulmonary circuit.

Vasculature

Vascular parameters of compliance and resistance were recreated by the use of windkessel vessels and proportional control pinch valves, respectively. Compliance was easily varied by vertically positioning a standard pipe test plug within the PVC pipe chambers to secure an amount of air above the fluid level and thus achieve the desired value of compliance. In the case of resistance, a change in control valve input voltage proportionally occludes the pipe.

To reproduce the compliant nature of blood vessels, arterial and venous chambers are plumbed into the circuit. Because the arteries and veins of the systemic and pulmonary systems encounter different pulse pressures, chambers of appropriate dimensions were used to recreate the desired compliances. Each chamber is closed to atmosphere and contains a certain volume of air above the fluid level. This volume of air controls the change in chamber pressure with the introduction of an extra volume of fluid into the chamber, as dictated by Boyle’s Law. Table 2 details specific mock loop compliance for rest and LHF as compared with natural values (10,19).

Resistance of arteries, capillaries, and veins are combined into a lumped systemic vascular resistance (SVR) and a pulmonic vascular resistance (PVR).
SVR and PVR are represented by the inherent resistance of the 32-mm PVC piping, check valves, and fittings and further refined by proportional control pinch valves (HASS Manufacturing, New York, NY, U.S.A.) situated between the arterial and venous chambers. The desired ranges of SVR and PVR for resting and heart-failure conditions are given in Table 3 (10, 20).

**Mock loop physiology**

To test the effect of VAD insertion on the cardiovascular system undertaken by Timms et al. (18), it is important to reproduce natural hemodynamic values of pressure and perfusion for each physiological condition of rest and LHF.

The natural values of resting-heart chamber and arterial pressure during systolic and diastolic periods are identified graphically in Fig. 3. These values are tabulated for comparison to mock loop results in Table 4 (10, 11). The time trace of pressure distribution in the heart and arteries (Fig. 4) characterizes the trend over a single cardiac cycle while illustrating the relative difference in magnitude between left and right systems. These pressure ranges are created in the mock loop by contraction of the artificial ventricles and maintained by appropriate compliance and resistance values.

### Table 3. Resistance values

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Natural</td>
<td>Mock</td>
</tr>
<tr>
<td>SVR</td>
<td>1463</td>
<td>1439</td>
</tr>
<tr>
<td>PVR</td>
<td>106</td>
<td>133</td>
</tr>
</tbody>
</table>

### Table 4. Pressures values

<table>
<thead>
<tr>
<th>mm Hg</th>
<th>Rest</th>
<th>Heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Natural</td>
<td>Mock</td>
</tr>
<tr>
<td>LAP</td>
<td>8–10</td>
<td>8–10</td>
</tr>
<tr>
<td>LVP</td>
<td>0–120</td>
<td>0–120</td>
</tr>
<tr>
<td>LVP_{ED}</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>AoP</td>
<td>120/80</td>
<td>119/78</td>
</tr>
<tr>
<td>MAP</td>
<td>93</td>
<td>96</td>
</tr>
<tr>
<td>RAP</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>RVP</td>
<td>0–25</td>
<td>0–32</td>
</tr>
<tr>
<td>RVP_{ED}</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>PAP</td>
<td>25/10</td>
<td>26/11</td>
</tr>
<tr>
<td>MPAP</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td>P_{mc}</td>
<td>7</td>
<td>7</td>
</tr>
</tbody>
</table>

LAP, left atrial pressure; LVP, left ventricle pressure; LVP_{ED}, left ventricle end diastolic pressure; AoP, aortic pressure; MAP, mean aortic pressure; RAP, right atrial pressure; RVP, right ventricular pressure; RVP_{ED}, right ventricular end diastolic pressure; PAP, pulmonary arterial pressure; MPAP, mean pulmonary arterial pressure; P_{mc}, mean circulatory pressure.
targeted for reproduction in physiological conditions of rest and LHF (7). These perfusion rates are monitored via two electromagnetic flow meters (IFC010, Krohne, Duisburg, Germany).

Reproduction of rest and heart-failure conditions

The physiological conditions of simulated rest and heart failure are reproduced by altering $P_{mc}$, heart contractility, heart rate, vascular resistances, and arterial compliance. The aim was to mimic the natural hemodynamic and autoregulatory response to changes in heart function and medical drug therapy. For example, from a healthy resting ventricle, cardiac function is depressed in cases of heart failure, and cardiac output falls. The natural response of the cardiovascular system is to increase heart rate, increase blood volume, reduce compliance, and increase SVR to raise cardiac output at the expense of elevated right atrium (RA) pressures (10,11). The elevated SVR response ultimately increases the heart’s workload and limits perfusion. Medical drug therapy for treatment of heart failure reduces heart rate and increases perfusion, by reducing vascular resistance at the expense of mean arterial pressure.

EXPERIMENTAL PROCEDURE

CONTROLDESK was used as an interface to a SIMULINK model that communicated with the rig via the dSPACE controller board. This enabled the real-time capture of hemodynamic variables (flow and pressure) and control of vascular and heart parameters (vascular resistance, heart rate/systolic period).

The mock circulation rig was configured to operate in a complete circulation mode to evaluate hemodynamic performance for resting and heart-failure conditions. Compliance values described in Table 2 were established by positioning the test plugs at a vertical distance from the top of each chamber. Small piping holes through the test plugs were capped by the pressure transducers and a bleed valve. This valve was opened to equalize chamber pressure with atmospheric pressure. The rig was then filled with approximately 5 L water. This volume filled the piping and raised the water level to 40 mm above the bottom of each compliance chamber. At this point, the bleed valves were closed, trapping a predetermined volume of air above each fluid level. An additional volume of fluid was then added to the left and right atrial chambers. Due to the compliance of all chambers, this extra volume slightly compressed the air in each chamber. Water was added until the desired $P_{mc}$ for rest or LHF was reached. Left and right air compressors were charged. The output regulator of the left compressor was changed to reflect the simulated degree of left heart functionality. The ventricular chamber input regulators were tuned to the maximum left ventricle pressure and right ventricle pressure. The heartbeats were then initiated. The CONTROLDESK interface enabled the selection of heart rate and systolic period (Table 1), which signaled each solenoid valve operation. Vascular resistance (Table 3) was finally tuned to reproduce the desired hemodynamic response.

RESULTS

Results were obtained to verify the ability of the mock loop to recreate the hemodynamic characteristics of the natural circulatory system. Complete mock loop results for normal and left heart-failure simulations are presented for comparison with natural cardiovascular hemodynamics. Systemic and pulmonary pressure distributions for each condition are presented in Figs. 5 and 6, respectively. The left side in each figure details all component pressures over a single cardiac cycle, while the three graphs on the right side demonstrate the stability of individual component pressure over four cardiac cycles. Systemic (Fig. 7) and pulmonary (Fig. 8) perfusion rates are also displayed over four cycles, indicating pulsatile flow and mean perfusion rates.

Pressures recorded in the systemic and pulmonic loops for resting conditions are recorded in Table 4 and graphically displayed in Figs. 5 and 6, respectively. A mean aortic pressure (MAP) of 96 mm Hg and pulmonary arterial pressure (PAP) of 17 mm Hg was observed in the circuit. Left atrial pressure (LAP) varied from 8 to 10 mm Hg, while right atrial pressure (RAP) oscillated about 4 mm Hg. Simulated LHF encountered an expected decline in MAP (60 mm Hg) and a rise in PAP (30 mm Hg). LAP was also predictably higher (20 mm Hg), indicating a degree of pulmonary congestion. Considerable transient pressure fluctuations were observed in the artificial atrial and ventricular chambers. These occurrences were attributed to water-hammer surges caused by the rigidly mounted and rapidly closing brass swing check valves. These relatively high frequency fluctuations were digitally filtered in real time. A phase shift was also observed between ven-
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tricular and arterial pressure measurements. This was attributed to wave reflections and inherent inertial effects of the mock vasculature, due to the piping cross-sectional areas and lengths, coupled with vascular chamber dimensions.

Systemic and pulmonic perfusion rates are displayed in Fig. 7 for simulated resting and Fig. 8 for left heart-failure conditions. In this setting, perfusion was reduced from a normal resting value (5.15 L/min) to those expected during LHF (2.7 L/min).

The rig’s adherence to Frank-Starling law is by design and, although not quantitatively measured, was qualitatively observable during operation. Changes in preload were observed through the clear PVC piping as changes in ventricular chamber fluid level prior to systole. A consequent change in stroke volume was also observed through these chamber walls.

DISCUSSION

The results demonstrate the ability of the complete mock system to reproduce resting physiological functions of the heart and vascular systems for normal and medically treated failing heart function.

The pneumatic technique of introducing compressed air into the ventricles to recreate the heart’s function was successful in reproducing the heartbeat. The solenoid valves, controlled by CONTROLDESK and dSPACE card, enabled the successful recreation of heart rate to 60 bpm and systolic period to 40% in both resting and LHF simulations.

FIG. 5. Systemic (A) and pulmonic (B) vascular pressure distribution for normal (healthy) resting conditions. AoP, aortic pressure; LAP, left atrial pressure; LVP, left ventricle pressure; MAP, mean aortic pressure; MPAP, mean pulmonary arterial pressure; PAP, pulmonary arterial pressure; RAP, right atrial pressure; RVP, right ventricular pressure.

FIG. 6. Systemic (A) and pulmonic (B) vascular pressure distribution for heart-failure conditions. AoP, aortic pressure; LAP, left atrial pressure; LVP, left ventricle pressure; MAP, mean arterial pressure; MPAP, mean pulmonary arterial pressure; PAP, pulmonary arterial pressure; RAP, right atrial pressure; RVP, right ventricular pressure.
These values are comparable to normal heart function at rest. However, untreated heart failure demonstrates a lower systolic period and a higher heart rate. Nevertheless, heart-failure treatment with drug therapy attempts to return these parameters back to normal, as simulated in this study. Heart rate can be increased to up to 120 bpm by altering solenoid parameters; however, perfusion is limited in the complete loop due to the minimum pulmonary circuit resistance. Replacement of the current flow meter in this circuit with a larger diameter flow meter would alleviate this problem and allow the reproduction of a wider range of hemodynamic conditions.

The regulators at ventricular entrance limited ventricular maximum pressure. The maximum pressure set on the right ventricle regulator was higher than anticipated, to provide sufficient air mass flow rate for normal right-heart function. Because the air is only input for a short amount of time, the ventricular pressure did not rise above 40 mm Hg.

The natural ventricle is characterized as a chamber encountering a decreasing compliance during the systolic phase. The pneumatic technique of heart functionality reproduced this characteristic by introducing air into an initial, presystolic ventricular chamber air volume above the fluid level. The additional air increased the pressure within the ventricle in proportion to the rate of air inflow, according to Boyle’s law. This provided the ability to easily vary the degree of heart function to simulate all physiological conditions by varying input air mass flow rate.

The natural heart has the ability to alter contractility in response to changes in preload. This preload is determined by the majority of venous return passively filling the ventricle during the diastolic phase. Passive filling ventricles are an important feature, because the natural heart is predominantly considered nonsucking and therefore relies on the atrial and venous pressures to refill the ventricle during diastole. In operation, an increase in preload due to increases in alternate ventricular function or $P_{mc}$ stretches the ventricular myocytes, enabling a more forceful systolic contraction. This is the guiding principle behind the Frank-Starling law and was qualitatively observed in the physical mock loop.

To explain further, an increase in ventricular preload resulted in an observably higher fluid level within the clear-walled ventricular chamber. This effectively reduced the volume of air contained within the chamber above the fluid prior to the subsequent systolic period. An increase in contractility resulted, as the time for pressure rise in the smaller air volume for the same input mass flow rate is lower, and therefore the observable stroke volume increased. This effect is reversed for cases of reduced preload.

The brass check valves performed the function of each heart valve by providing low resistance to forward flow as well as sufficient restriction of back flow. However, the weight of the swing and its metallic nature, and hence inherent noncompliance, caused significant pressure spikes and oscillations within the ventricle attributed to water-hammer effects and bouncing of the swing. This effect was reduced by placing a low-pass filter on the ventricular pressure recordings.

Pressures recorded in the mock loop are compared to the natural cardiovascular pressure distribution in the following figures:

**FIG. 7.** Perfusion rate for normal heart function. MPQ, mean pulmonary flow rate; MSQ, mean systemic flow rate; PQ, pulmonary flow rate; SQ, systemic flow rate.

**FIG. 8.** Perfusion rate for left heart failure. MPQ, mean pulmonary flow rate; MSQ, mean systemic flow rate; PQ, pulmonary flow rate; SQ, systemic flow rate.
Table 4. Ventricular pressures were successfully transferred to the arterial chambers, with any phase delay attributed to wave speed, wave reflection, and vasculature inertial effects. This vasculature inertia is a topic for further investigation. It is important for the mock loop to recreate the characteristic input impedance (12), and preliminary studies of input iner tance revealed similar values to those experienced in the natural circulatory system. Waterhammer surges excessively raised the ventricular pressure in the early systolic phase. These superimposed pressure transients were suppressed by imposing a digital filter on the recorded pressure data. The planned introduction of an appropriately sized accumulator near the valves would physically reduce these transients, thus reducing the need for this digital filtering. The response of the arterial pressure wave was affected by the compliance value and the entrance/exit resistance into each chamber. These parameters also dictated pulse pressure. Venous pressures were maintained at reported physiological levels due to the larger compliance chamber employed, thus allowing sufficient venous return to the left and right ventricles and helping to maintain correct atrial pressures and consequently ventricular preload. The introduction of extra fluid was successful in modifying the $P_{inc}$ higher in heart-failure cases.

Compliance values of individual mock loop component chambers were recreated reasonably close to the ranges expected in the natural circulatory system. Arterial compliances were slightly higher to account for the inertial effects of the mock vasculature, thus maintaining expected pulse pressures. Systemic compliance was reduced in the LHF case, as dictated by the natural regulatory response to heart failure.

Values of natural vascular resistance were faithfully reproduced within the mock vasculature for the resting condition. However, for simulated LHF, resistance was considerably lower than those values created by the autoregulatory response. The discrepancy is attributed to the degree of heart failure and simulated treatment. Higher values of resistance represent the typical natural autoregulatory response to heart failure. However, medical drug treatment of heart failure attempts to reduce the SVR to values approaching rest for normal heart function. This action reduces the workload on the heart and results in increased perfusion at the expense of MAP.

Under normal and failing heart functions, perfusion rates were found to pulse with each cardiac cycle, averaging to flow rates consistent with reported values for both conditions (Figs. 7 and 8). However, maximum flow pulses for each system are somewhat reduced due to the time constant of the flowmeter and the technique of lumping and controlling the vascular resistances with one pinch valve only.

**CONCLUSION**

The techniques employed to recreate the complete human circulatory system provided an accurate method of simulating physiological pressures and perfusion throughout the cardiovascular network for resting normal and medically treated failing heart function. The left or right ventricular heart function could be independently and variably controlled. The Frank-Starling response to all physiological conditions was observed in the developed rig, due to the recreation of passive filling ventricles. Easily variable vascular parameters enabled the system to recreate natural hemodynamics in each condition. Furthermore, the rig demonstrated the hemodynamic effect of medical treatment.

The developed rig can be used as a cost effective method to evaluate the hemodynamic impact of left, right, and bi-VADs on the circulatory system.

Although the mock loop will never replace in vivo trials, by improving its performance, sufficient results may be obtained to refine VAD designs before these expensive trials.

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