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CHARACTERIZATION OF FLUID PHYSICS EFFECTS ON CARDIOVASCULAR RESPONSE TO MICROGRAVITY [G-572]

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ABSTRACT

The recognition and understanding of cardiovascular adaptation to spaceflight has experienced substantial advancement in the last several years. In-flight echocardiographic measurements of astronaut cardiac function on the Space Shuttle have documented a 15% reduction in both left ventricular volume index and stroke volume with a compensatory increase in heart rate to maintain cardiac output. To date, the reduced cardiac size and stroke volume have been presumed to be the consequence of the reduction in circulating fluid volume following diuresis and other physiological processed to reduce blood volume within a few days after orbital insertion. However, no specific mechanism for the reduced stroke volume has been elucidated. The following investigation proposes the use of a hydraulic model of the cardiovascular system to examine the possibility that the observed reduction in stroke volume may, in part, be related to fluid physics effects on heart function. The automated model is being prepared to fly as a GAS payload.

The experimental apparatus consists of a pneumatically actuated, elliptical artificial ventricle connected to a closed-loop, hydraulic circuit with compliance and resistance elements to create physiologic pressure and flow conditions. The ventricle is instrumented with high-fidelity, acceleration-insensitive, catheter-tip pressure transducers (Millar Instruments) in the apex and base to determine the instantaneous ventricular pressures and ΔP_{LV} across the left ventricle (LVP_{apex} - LVP_{base}). The ventricle is also instrumented with a flow probe and pressure transducers immediately upstream of the inflow valve and downstream of the outflow valve. The experiment will be microprocessor controlled with analog signals stored on an FM data tape recorder. By varying the circulating fluid volume, ventricular function can be determined for varying preload pressures with fixed afterload pressure. Pilot experiments on board the NASA KC-135 aircraft have demonstrated proof-of-concept and provided early support for the proposed hypothesis. A review of the pilot experiments and developmental progress on the GAS version of this experiment will be presented.

INTRODUCTION

The objective of the proposed research is to clarify the role of fluid physics effects on cardiovascular response to the microgravity environment using physical and analytical modeling techniques. Specifically, the role of the gravitationally-dependent, intraventricular hydrostatic pressure difference in ventricular filling will be investigated. The proposed investigation is stimulated by the results of in-flight echocardiographic measurements of astronaut cardiac function on the Space Shuttle[1]. These echocardiographic measurements have documented a 15% reduction in both left ventricular volume index and stroke volume with a compensatory increase in heart rate to maintain cardiac output. To date, the reduced cardiac size and stroke volume have been presumed to be the consequence of the reduction in circulating fluid volume following diuresis and other physiologic processess to reduce blood volume within a few days after orbital insertion.[2,3] However, no specific mechanism for the reduced stroke volume has been elucidated. The following investigation proposes the use of a hydraulic model of the cardiovascular system to examine the possibility that the observed reduction in stroke volume may, in part, be related to fluid physics effects on heart function.

Many biophysical factors influence the filling of the heart during diastole. These factors include (1) the atrial pressure, (2) the inertia energy of the blood as it enters the ventricle, (3) the transmural pressure gradient, (4) the diastolic compliance of the myocardium and the passive, elastic recoil attributed to the "parallel elastic element" connective tissue mesh around the myofibrils,[4,5] and (5) a factor recently recognized,[6] a gravitational acceleration-dependent hydrostatic pressure difference, ΔP, that exists in the ventricles due to their size and anatomic orientation to the local gravitational axis. This investigation is limited to an examination of left ventricular function although the same concepts apply to right ventricular function. Hence, only the hydrostatic pressure difference in the left ventricle, ΔP_{LV}, will be considered in the proposed research. This hydrostatic ΔP_{LV} linearly increases the intraventricular pressure when progressing from the ventricular base to apex (Figure 1). Consequently, the linearly increasing ΔP_{LV} acts to augment the diastolic filling of the heart by increasing the elongation of the elastic, contractile, and viscous elements of the ventricular wall. The hydrostatic ΔP_{LV} is the product of the blood density ($\rho_{blood} = 1.06$ gm/cm^3), gravitational acceleration constant ($g = 980$ cm/sec^2), and the change in fluid column height from the reference point (Δh_{LV} cm). MRI scanning data has indicated that a typical Δh_{LV} for an average adult male left ventricle is approximately 7 cm. This Δh_{LV} results in a ventricular base-to-apex ΔP_{LV} of ≈ 7300 dynes/cm^2 (≈ 5.5 mm Hg) for an average effect of between 2 to 3 mm Hg. Consequently, based purely on fluid physics considerations, in the absence of gravity where ΔP_{LV} becomes zero one would predict a reduced ventricular filling and therefore reduced stroke volume resulting in a rightward shift of the ventricular function curve (output vs. ventricular filling pressure) of 2 to 3 mm Hg. Hence, the investigators have hypothesized that the absence of ΔP_{LV} in the microgravity environment of spaceflight may account, in part, for the 15% reduction in stroke volume reported for astronauts while in orbit. An experimentally observed shift of ventricular function curve to the right during exposure to the microgravity environment would support the hypothesis of this experiment.

The objective of this research program will be addressed by the collection of cardiac performance data from a flight-worthy hydraulic model of the cardiovascular system in the extended duration, higher quality microgravity environment of orbital flight as a Get Away Special payload for the anticipated follow-up program. The results will influence the conduct and direction of future investigations into cardiovascular response to microgravity by recognizing the role of fluid physics effects. The investigators anticipate that the development of a three-dimensional, anatomically consistent hydraulic model will expand into other areas of investigation, such as changes in regional hemodynamics and fluid shifting with changes in posture (e.g. vertical vs. launch position). This study will advance the understanding of cardiovascular response to the environments experienced in manned spaceflight.

DEVELOPMENTAL PROGRESS AND METHODS

REVIEW OF THE PILOT EXPERIMENT CARDIOVASCULAR MODEL

Proof-of-concept for the proposed GAS payload was achieved by flying a pilot experimenton board the NASA KC-135 aircraft. The results and lessons learned from the pilot experiments have guided the development of the GAS version of the experiment. The hydraulic model of the cardiovascular system for the pilot experiment consisted of a pneumatically actuated, elliptical artificial ventricle (UTAH-100 human version left ventricle,[7,8] 5cm x 6cm x 10cm) with prosthetic mitral and aortic valves (Medtronic Hall™, Medtronic, Inc.) and a highly compliant, pumping diaphragm. The inflow and outflow ports were located at the superior end of the long-axis of the ventricle to approximate the anatomy of the natural left ventricle (Figure 2). A compliant artificial atrium was attached upstream of the inflow port of the ventricle. The ventricle was connected to a closed-loop, hydraulic circulation simulator (an adapted version of the Penn State mock circulation[9]) with compliance and resistance elements to create physiologic pressure and flow conditions (Figure 3). The mock circulation was filled with a blood-analog fluid of 40% glycerin in water to approximate the viscosity of whole blood (3.4 cP @ 115 sec^{-1}). The mock circulation was fixed to a stainless steel tray (1m x 1.5m x .1m) which, in turn, was bolted to a floor-mounted support frame secured to the floor of the NASA KC-135 research aircraft.

The ventricle was instrumented with high fidelity, acceleration-insensitive, catheter-tip pressure transducers (Millar Instruments) in the apex and base to determine the instantaneous ventricular pressures and ΔP_{LV} across the left ventricle (LVP_{apex} - LVP_{base}). When the ventricle was positioned at 45° to the horizon to mimic the anatomic orientation of the human left ventricle, the Δh_{LV} for the UTAH-100 left ventricle was 6.3 cm, resulting in a calculated base-to-apex ΔP_{LV} of 4.9 mm Hg. The ventricle was also instrumented with flow probes (Transonic Systems) and pressure transducers (Millar Instruments) immediately upstream of the mitral valve (inflow) and downstream of the aortic valve (outflow, see Figure 2). Pressure transducers and flow probes and their calibration signals were calibrated against reference standards prior to shipment of the hardware to Ellington Field and upon return to Salt Lake City. The electrical calibration reference signals were used for in-plane checks of probe calibration. The shearing rate profile of the glycerin/water blood-analog fluid was also verified prior to departing Salt Lake City using a cone-and-plate viscometer (Brookfield Engineering, Model LVTDV-IICP).

The associated recording equipment and heart controller was rack-mounted in a chassis that was fixed to the aircraft floor. The equipment in the chassis included: a sixteen-channel digital data tape recorder (TEAC, Model RD-200T); a two-channel flow meter (Transonic Systems); eight transducer pre-amplifiers (Gould); an eight channel thermal pen recorder (Gould); and an artificial-heart controller (CardioWest Technologies) with a regulator and two tanks of compressed air. Accelerometers (PCB Piezotronics, Kistler) to measure the vertical axis (G_z) acceleration were mounted on the instrumentation chassis and the circulation simulator tray. The instrumentation chassis was five feet tall and weighed 441 pounds; the hydraulic simulator of the cardiovascular system with mounting tray and cart was three feet tall and weighed 160 pounds.

The in-flight test protocol specified the examination of ventricular function with the heart rate fixed at 90 beats per minute to correspond to the elevated heart rates reported for orbital flight.[2,3] The percentage of the cardiac cycle spent in systole was 43% and the ventricular driveline pressure delivered to inflate the diaphragm was 190 mm Hg. This driveline pressure was sufficient to fully eject whatever stroke volume the preload conditions created while the ventricle pumped against a mean afterload pressure of 95 mm Hg during stable, 1-G flight. Since this mode of artificial ventricular control (referred to as partial-fill, full eject) results in the same end-systolic volume at a fixed heart rate, any changes in the cardiac output are due to a change in stroke volume and, therefore, diastolic function. The circulating fluid volume of the mock circulation could be adjusted to create different preload conditions on the ventricular function curve. In-flight, the initial circulating fluid volume was adjusted to establish a stable, 1-G baseline near the peak of the ventricular function curve. After each set of 10 parabolas, 60 ml of the blood-analog fluid was withdrawn from the circulating fluid volume to establish a new, lower preload condition. The pressure, flow, and acceleration signals were continuously recorded to document the hemodynamic changes during the transition from 1-G to microgravity, during the period of microgravity, and during the transition from microgravity back to 1-G (including the period of ≈ 1.8-G hypergravity). The mock circulation system stabilized at a new operating condition in approximately 5 seconds, so steady system function was achieved for the majority of the 20 second duration microgravity exposure period. Data from 10 consecutive beats at equilibrium test conditions were used to create ventricular function curves for each of the test conditions as well as to examine the end-diastolic pressure difference between the left ventricular base and apex.

The pilot experiments on board the NASA KC-135 have demonstrated proof-of-concept and provided early support for the proposed hypothesis as the predicted rightward shift of the ventricular curve was observed[6]. However, it was learned from the initial KC-135 experiments that (1) the ability to test over a range of preload conditions was limited, (2) aircraft vibration artifact diminished the quality of the data obtained, and (3) the hydraulic model needed refinement as indicated by the lack of rigorous physiologic authenticity of the instantaneous pressure and flow waveforms. All of these lessons learned have indicated the need for additional model development for the GAS version of the experiment.

GAS PAYLOAD DEVELOPMENT

The proposed research program requires the performance of three main tasks: (1) refinement of the cardiovascular system hydraulic model using both analytical modeling and physical testing (2) automating the function of the cardiovascular system hydraulic model, and (3) modifying the experimental apparatus to be compatible with the weight, space and operational specifications for a GAS payload.

The tasks pertaining to the refinement of the cardiovascular system hydraulic model are driven by two criteria:

(1) improving the dynamic response of the model and the physiologic authenticity of the instantaneous outflow pressure and flow waveforms (as validated by comparing the resulting input impedance spectra to the human spectra[10]); and

(2) accommodating the elements of the hydraulic model within the space limitations (19.75" diameter x 28.25" height) and weight limitation (200 pounds) for a Get Away Special payload canister.

Improving the dynamic response of the model and the physiologic authenticity of the instantaneous outflow pressure and flow waveforms will be accomplished by:

(1) reducing the inertance in the hydraulic model by shortening the circuit length as much as possible and eliminating bends with small radii;

(2) addition of more circuit elements, such as a characteristic resistor in the proximal section of the outflow conduit; and

(3) changing the systemic resistance element from a static to a dynamically varying elements with feedback and control so as to maintain a constant mean outflow pressure regardless of the test condition.

Proposed changes to the hydraulic model will first be evaluated using an analytical modeling method described below which will predict whether the physiologic authenticity will be improved. Ground-based tests will then acquire outflow pressure and flow waveforms for the computation of the input impedance spectrum[10] to verify the prediction of the analytical modeling assessment.

Accommodating the elements of the hydraulic model within the space and weight limitations for a Get Away Special payload canister will be accomplished by:

(1) reducing the length of the hydraulic circuit;

(2) reducing the size of the compliance chambers;

(3) integrating the compliance and resistance elements, and other components when possible; and

(4) automatic changes of the circulating fluid volume with a microprocessor controlled, miniature infusion/withdrawal pump

The feasibility of approaches 1 and 2 has recently been demonstrating by (1) reducing the length of the circuit used in the pilot project hydraulic simulator (shown in Figure 3) and eliminating bends with small radii and (2) reducing the size of the compliance chambers as shown in Figure 4. By reducing the length of the hydraulic circuit, the physiologic authenticity of the outflow pressure and flow waveforms was dramatically improved as shown in Figure 5 and verified by a comparison of the input impedance spectra. Significant weight and size reduction of the compliance chambers was achieved by substituting the leaf spring mechanism with a coil spring mechanism while maintaining the desired physiologic compliance. The weight was reduced from 13.6 pounds to 7.7 pounds and the size was reduced from approximately 18x7x12 inches to 7x7x12 inches.

Analytical Modeling of the Hydraulic Model

Candidate changes to the cardiovascular system hydraulic model will be represented by lumped parameter models. These lumped parameter models will be tested by computer to find the best match of impedance to the human circulation. The strategy for choosing model configurations will be to optimize the response of the model, not to duplicate existing mock circulation systems. This will ensure that authenticity will be achieved. In general, for each element in the analytical model, one point on either the impedance modulus or phase plot may be matched exactly. The more elements in the model, the more perfect the match, but each matching point chosen represents an additional nonlinear algebraic equation which must be solved for the values of the elements. Poles and zeros are the easiest points for which to solve since many solutions of this type are available from the field of electrical engineering. However, modulus and phase at harmonics of the heart beat frequency are more relevant matching points for models of the circulation because these are the points for which data are available or can be calculated with Fourier analysis. Solutions derived preliminary to this proposal used the latter method. For models with more than a few elements, an iterative solution becomes necessary. A multi-dimensional Newton-Raphson iteration algorithm has already been written and verified for solution of element values for models with up to five elements[12]. This method has the advantage of fast convergence if a good initial estimate for the solution can be input. The number of dimensions which the algorithm will accommodate is not limited, although the solution becomes unstable for poor initial estimates on systems with many elements. Bounds on the solution were imposed and the magnitude of the incremental steps was controlled to promote stability. The Downhill Simplex method was used to provide good initial guesses and to verify the final solution. This method has the advantage of good stability, but the disadvantage of slow convergence. These two algorithms will form the basis for solutions for more complex models.

Solutions are not needed for extremely large numbers of elements, since physical systems representing complex analytical models would become difficult to adjust and operate. It is anticipated that a good impedance match can be attained with less than ten elements. Arriving at the optimum configuration of elements is largely a trial and error process, guided by experience. For each trial configuration, descriptive simultaneous algebraic equations must be written. Solutions are then obtained iteratively.

A numerical model will also be developed of the actual performance of the improved mock circulation system after it is finalized. Ideally, the mock circulation system response will conform to that of the lumped parameter model derived above, although small deviations are to be expected. This as-built computer model will be useful for simulation and prediction of device performance when connected to the mock circulation system. The same solution algorithms as discussed above will be used for this task. Again, the common goal of the proposed research plan is to utilize measured human vascular input impedance as a standard for the development of advanced analytic and hydraulic models. This approach has proven successful for the Co-P.I.[11,12] and has recently be corroborated by other investigators.[13]

GAS Payload and Protocol Description

Experimental methods to be employed for the proposed GAS payload will build on the methods developed for the pilot experiments. The revised hydraulic model of the cardiovascular system will use the same pneumatically actuated artificial ventricle used for the pilot experiment (Figure 4). A compliant artificial atrium will be attached immediately upstream of the inflow port of the ventricle. The ventricle will be connected to revised compliance and resistance elements (as mentioned in the previous section, Figure 4) to create improved physiologic pressure and flow conditions. The mock circulation will be filled with a blood-analog fluid of 40% glycerin in water to approximate the viscosity of whole blood (3.4 cP @ 115 sec^{-1}). A microprocessor-controlled peristaltic pump will infuse or withdraw fluid on command to create difference levels of circulating fluid volume and ventricular preload conditions to allow the generation of a ventricular function curve from the in-flight data.

The ventricle will be instrumented with high fidelity, acceleration-insensitive, catheter-tip pressure transducers (Millar Instruments) in the apex and base to determine the instantaneous ventricular pressures and ΔP_{LV} across the left ventricle (LVP_{apex} - LVP_{base}). The ventricle will also be instrumented with pressure transducers (Millar Instruments) immediately upstream of the mitral valve (inflow) and downstream of the aortic valve (outflow) and a flow probe (Transonic Systems) downstream of the outflow valve. Pressure transducers and flow probes and their calibration signals will be calibrated pre and post-flight against reference standards and the shearing rate profile of the glycerin/water blood-analog fluid will also be verified prior to filling the hydraulic model of the cardiovascular system.

Analog data will be recorded on a data tape recorder (TEAC, Model HR-30). A flow meter signal conditioning board (Transonic Systems) and pressure transducer pre-amplifiers (Millar) will be incorporated into the payload. A miniaturized artificial-heart driver (Heimes™ Portable Heart Driver, Symbion) will control the funcition of the artificial ventricle. An accelerometer (Endevco) to measure the vertical axis (G_z) acceleration will be mounted on the hydraulic model chassis.

The experiment package will be turned by a switch in the aft flight deck during a quiescent period of dead-drift gravity gradient mode. The in-flight test protocol will specify the examination of ventricular function with the heart rate fixed at 90 beats per minute to correspond to the elevated heart rates reported for orbital flight. The percentage of the cardiac cycle spent in systole will be 43% and the ventricular driveline pressure delivered to inflate the diaphragm will be 190 mm Hg. This driveline pressure will be sufficient to fully eject whatever stroke volume the preload conditions create while the ventricle pumps against a regulated mean afterload pressure of 95 mm Hg. Since this mode of artificial ventricular control (referred to as partial-fill, full eject) results in the same end-systolic volume at a fixed heart rate, any changes in the cardiac output are due to a change in stroke volume and, therefore, diastolic function. The circulating fluid volume of the mock circulation will be adjusted to create different six different preload conditions on the ventricular function curve by graded withdrawals and infusions of circulating fluid. In-flight, the initial circulating fluid volume will be adjusted to establish a stable baseline near the peak of the ventricular function curve. After three minutes of functioning at the established preload condition, a predetermined amount of the blood-analog fluid will be withdrawn from the circulating fluid volume to establish a new, lower preload condition. The pressure and flow signals will be continuously recorded to document the hemodynamic changes during the transition from one preload condition to the next. A brief "on-off-on" sequence of hydraulic model operation will be used to document the mean circulatory filling pressure of the model in the different acceleration test environments. The ventricular function test will be repeated pre and post-flight on the ground so that a the 1-G data set can be compared to the in-flight data.

Data Reduction and Analysis

Analog pressure, flow, and acceleration signals from all ground and in-flight experiments will be recorded on FM data tape cassettes. Data reduction and analysis will proceed by two methods. First, the temporal changes in the recorded variables will be presented in chart recording format achieved by playing the tape back into a high fidelity, thermal array chart recorder (Graphtec Mark 12 Data Management System DMS1000). Second, mean and dynamic values of recorded signals will be determined by first playing back the tape back into an analog-to-digital converter and storing the digitized waveforms on a computer (GW Instruments MacADIOS ADPO A/D Converter, Macintosh IIci Computer, sampling rate of 716 Hz.) and then recalling the stored digital signals for subsequent manipulation to calculate desired values. Mean values to be determined from the stored digital signals include inflow pressure, left ventricular end-diastolic pressures (LVEDP) at the base and apex, the difference between the LVEDP at the base and apex, the mean outflow pressure, the mean outflow, and the stroke volume. These values will be determined for ten consecutive beats which occur after the response of the system to a change in gravitational acceleration has decayed The mean and standard deviation of the values will then be determined. A t-test will be used to assess the presence of statistically significant differences ($p<0.05$) between corresponding variables from the 1-G and µ-G test environments.

A linear regression, including correlation coefficient and significance level, will be determined for the ventricular function curves (stroke volume vs. $LVEDP_{base}$) from the 1-G and µ-G test environments. Tests of statistical significance of the differences between the zero-intercepts and the slopes of the regression lines will also be conducted.

The digitized outflow pressure and flow signals will also undergo harmonic decomposition using Fourier analysis to determine the input impedance spectrum (i.e., frequency dependent fluid resistance to fluid flow, where Z = oscillatory pressure/oscillatory flow) from the 1-G and µ-G test environments. The presence of statistically significant differences between impedance spectra will be tested using analysis of variance with repeated measures techniques.

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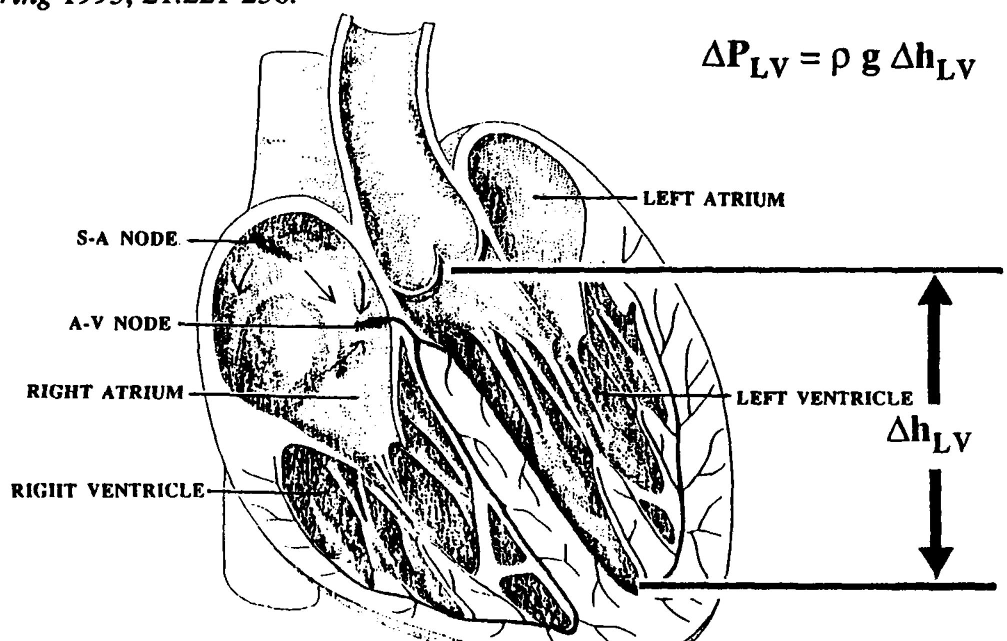


Figure 1. The intraventricular hydrostatic pressure difference, ΔP_{LV}, arises from the difference in height between the left ventricular base and apex as indicated by Δh_{LV}. This pressure difference is calculated using the equation: $\Delta P_{LV} = \rho g \Delta h_{LV}$, where ρ is the blood density (ρ_{blood} =1.06 gm/cm^3), g is the gravitational acceleration constant (g = 980 cm/sec^2), and Δh_{LV} is the change in fluid column height from the reference point in cm.

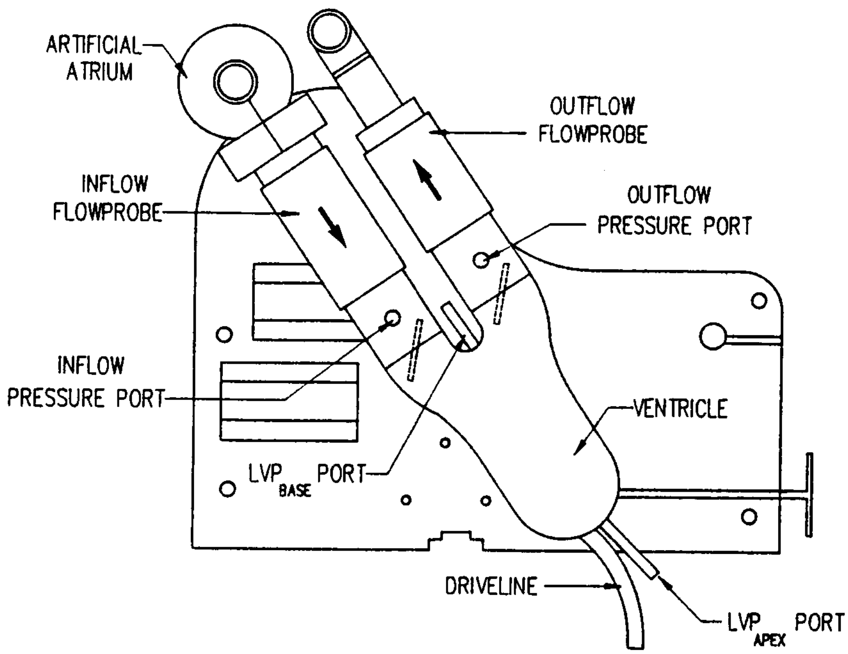


Figure 2. The artificial left ventricle used in the pilot experiments is shown positioned in the 45°, "1-G anatomic" orientation. The schematic indicates the location of the flow probes, pressure catheter introducer ports and other details. The arrows indicate the direction of flow through the ventricle.

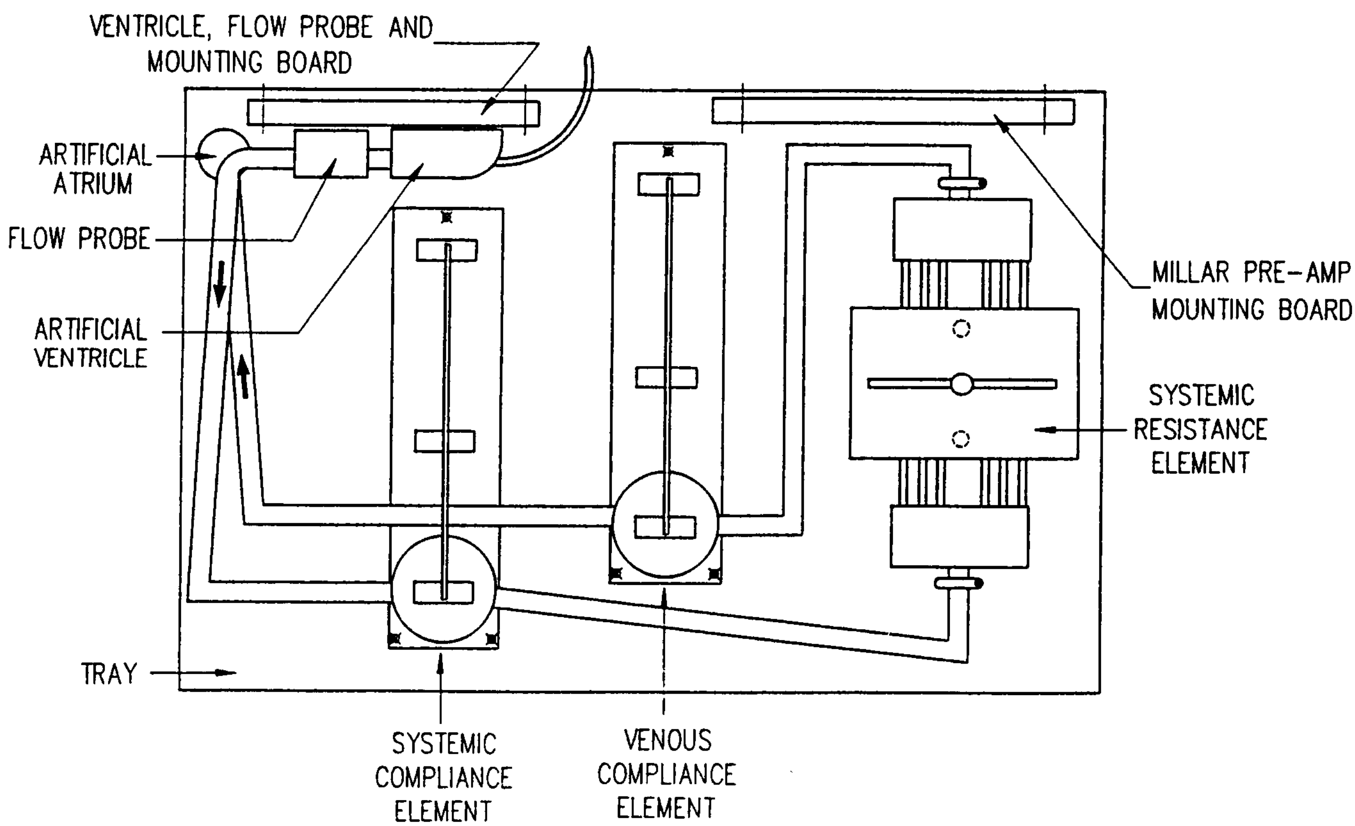
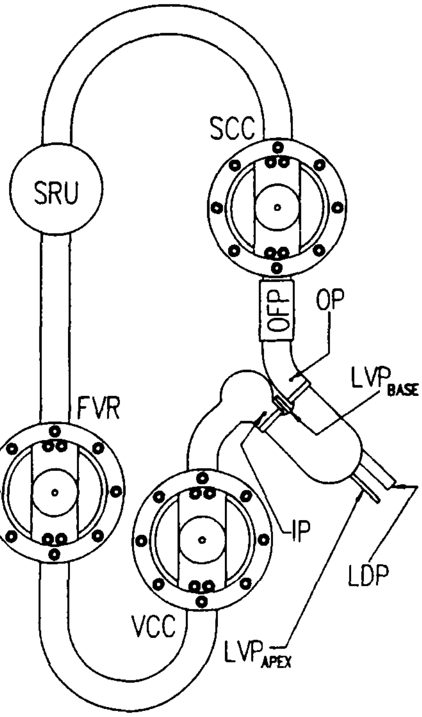


Figure 3. The hydraulic model of the cardiovascular system used in the pilot experiments is shown. The schematic indicates the location of the resistance and compliance elements as well as the artificial atrium and ventricle. The arrows indicate the direction of flow through the circulation simulator.



GAS PAYLOAD G-572 CONTENTS

COMPONENT	MAX POWER REQ.	WEIGHT LBS/(KG)
SCC=SYSTEMIC COMPLIANCE CHAMBER	- 0 -	7.7/(3.5)
SRU=SYSTEMIC RESISTANCE UNIT	TBD	2.0/(0.9)
PHD=PNEUMATIC HEART DRIVER	13.2V, 4A	13.2/(6.0)
FVR=FLUID VOLUME RESERVOIR	TBD	7.7/(3.5)
VCC=VENOUS COMPLIANCE CHAMBER	- 0 -	7.7/(3.5)
AH =ARTIFICIAL HEART	- 0 -	0.4/(0.2)
PRESSURE PRE-AMPS (5)	5.4V ea, 3.8 A 27V total	0.9/(0.4) ea 4.5/(2.0) total
FLOW PROBE	±5V, 200 mA	0.2/(0.1)
FLOW PROBE INTERFACE BOARD	±15V, 650 mA	0.5/(0.2)
DATA TAPE RECORDER	9V, 80 mA	1.3/(0.6)
EXPERIMENT CONTROLLER	TBD	TBD
BATTERIES	TBD	TBD
PRESSURE CATHETERS (5)	- 0 -	0.1/(.05)ea 0.5/(.25)total
AH DRIVELINE	- 0 -	0.2/(0.1)
CIRCULATING FLUID	- 0 -	2.2/(1.0)
CIRCUIT CONDUITS	- 0 -	1.1/(0.5)
CIRCULATION CONTAINMENT CHAMBER	- 0 -	TBD
ACCELEROMETER	TBD	TBD
A/D CONVERTOR & DIGITAL STORAGE	TBD	TBD
TEMPERATURE SENSOR	TBD	TBD
PASSIVE THERMAL INSULATION	TBD	TBD
INFUSION/WITHDRAWAL PUMP	TBD	TBD
FLUID RESERVOIR CONTAINER	TBD	TBD
STEPPER MOTOR	5V, 2A	TBD
HEATING ELEMENT	TBD	TBD
GCD INTERFACE	TBD	TBD
ELECTRICAL PLUMBING	- 0 -	TBD
BUMPERS	- 0 -	TBD
MOUNTING HARDWARE	- 0 -	TBD

Figure 4. The modified hydraulic model to demonstrate the feasibility of improving the physiologic authenticity and reducing the size of the pilot experiment hydraulic model is present along with the estimated weight and power budget for the GAS version of the experiment.

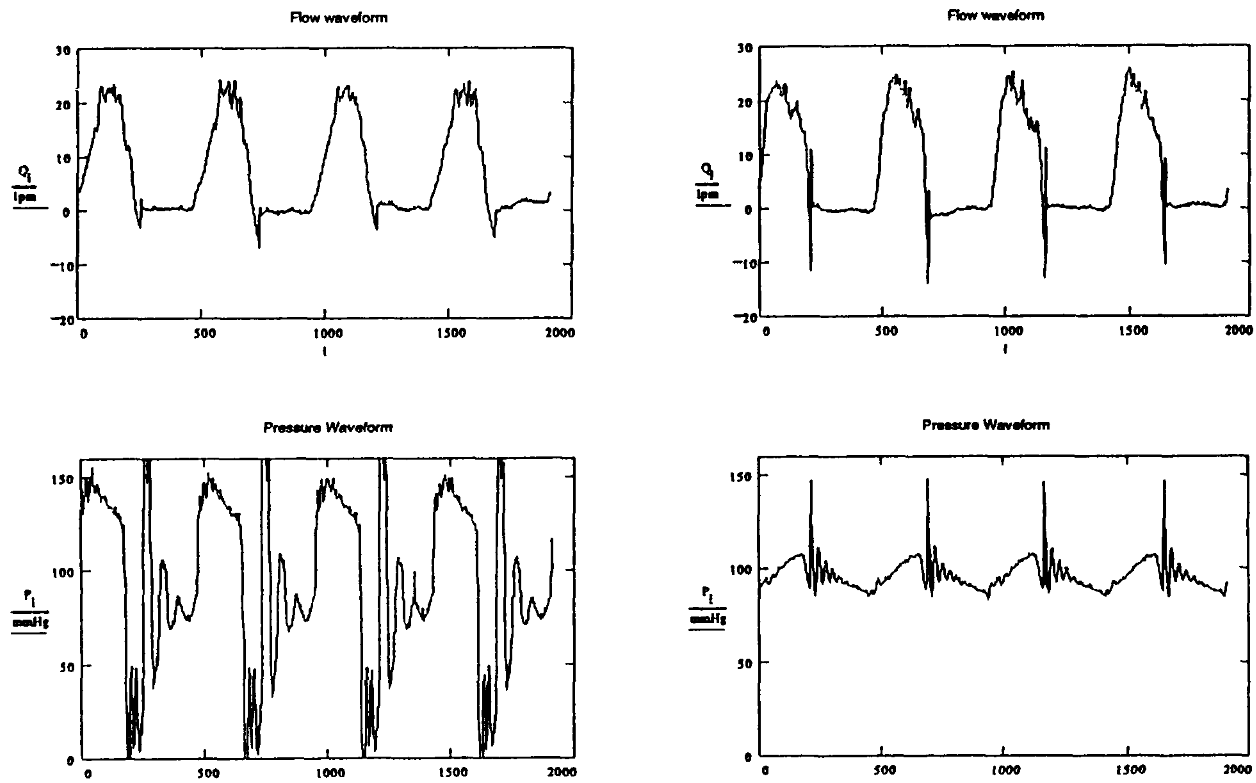


Figure 5. An example of the pilot experiment hydraulic model outflow pressure (bottom) and flow (top) waveforms are presented on the left for comparison to the improved outflow pressure and flow waveforms of the refinement feasibility hydraulic model presented on the right. The waveforms on the right are much more physiologic in appearance.