



Design of a Clinically Realistic CHF Model

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I Executive Summary

The purpose of our project is to develop, design and prototype a model of the left ventricle of a patient suffering from congestive heart failure. The model must be clinically realistic and satisfy specific engineering requirements.

Congestive heart failure (CHF), the primary motivation behind this project, is a disease that affects many people worldwide. It can be diagnosed as an inability of the heart to maintain an adequate circulation of blood throughout the body. It is characterized by the thinning and weakening of the left ventricle wall, the chamber of the heart which is responsible for providing blood to the body. Common treatments include lifestyle changes as well as drug therapy.

Our project will assist in treatment of CHF as it will enable preclinical testing of catheters used to deliver gene therapy to the left ventricle and serve as a model in which in vivo fluid mechanics through the vascular system can be studied.

Our primary design requirements include creation of pulsatile flow, visualization of catheter navigation, resemblance of CHF geometry, LV wall motion, incorporation of heart valves, and perfusion of a blood analog at body temperature.

The design concept we have selected as a pumping mechanism involves a rigid chamber filled with a water medium. The ventricle is suspended in the medium and a Harvard pump apparatus is used to create negative and positive pressures in the chamber, thereby causing the ventricle to expand and contract. A supply reservoir provides flow into the ventricle through a unidirectional mitral valve and fluid is pumped out through the aortic valve into an outflow reservoir. When complete, the system will also allow for the incorporation of Guidant's vascular model.

This quarter, the team focused on gathering background information, selecting a design concept, and prototyping the ventricle model and the flow system. The flow system involved the purchase of materials as well as the fabrication of the chamber at the Project Realization Lab. Next quarter, design specifications of the chamber will be finalized, and the chamber will be outsourced for construction.

Initial ventricle prototypes involved coating a balloon with latex and an SLA model with urethane. Additionally, modifications were made to a CAD drawing of the ventricle which will be used for the creation of a mold. Next quarter, material testing as well as finite element analysis will be done to determine the exact wall thicknesses required to produce the desired physiological deformation of the ventricle. Final ventricle fabrication will also take place.

Our final deliverables will include a complete flow system that incorporates a deformable LV and Guidant's vascular model. A report and final presentation describing the development and evaluation of our device will also be submitted.

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3.1 Sponsor Background

Guidant Corporation is one of the leading companies in medical device design for cardiovascular disease. Technology designed and produced by Guidant improves lives of patients suffering from heart failure and vascular conditions all around the world. Some of their products include pacing systems, guiding wires and catheters, abdominal aortic aneurysm repairs, coronary stent systems, as well as numerous other peripheral treatment products. Since its advent in 1994, Guidant has grown substantially, with revenues exceeding \$ 2.7 billion and an employee estimated at 9000. It has locations throughout Europe, Australia and the United States, with its corporate headquarters in Indianapolis, Indiana. One of its largest locations here in Santa Clara, California is involved in vascular intervention and minimally invasive treatment methods. As Guidant continues to grow, it shares its success with its employees, shareholders and community.

3.2 Clinical Background

The heart, shown in Figure 1 [8], is a four-chambered, muscular organ that pumps blood throughout the body. It is the power supply of the circulatory system, which provides oxygen and nutrients, in addition to removing carbon dioxide and other waste products. The heart beats interminably, allowing the myocardium, or heart muscle, to rest for a fraction of a second between beats.[8]

Due to the great demands upon the heart throughout a human lifespan, it is susceptible to failure, primarily left ventricular (LV) failure. Two major causes of heart failure are 1) coronary artery disease which leads to damage of the heart muscle (i.e. myocardial infarction) and 2) prolonged pumping against a chronically increased afterload as in the case of hypertension [5,9]. Backward failure occurs as blood that cannot enter and be pumped out by the heart continues to dam up in the venous system; forward failure occurs simultaneously as the heart fails to pump an adequate amount of blood forward to the tissue; the resulting congestion in the

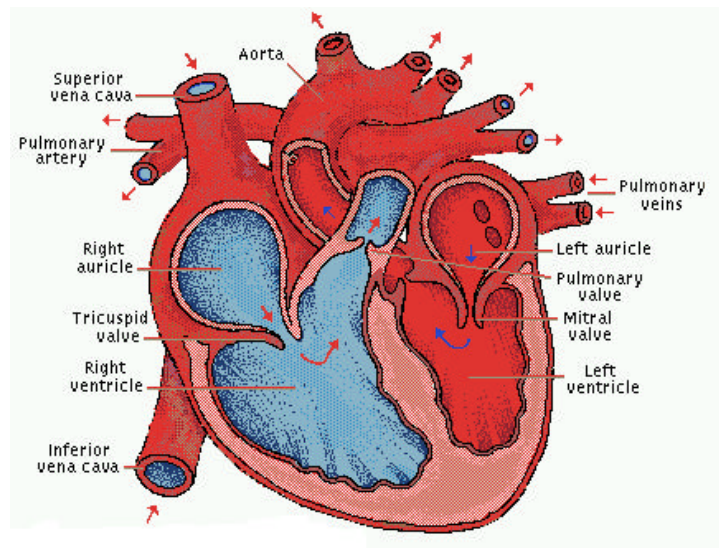


Figure 1: Schematic of the Heart. This diagram shows the chambers and valves of the human heart.

venous system is the reason this condition is called congestive heart failure (CHF) [9]. It is estimated that greater than 5 million Americans currently suffer from CHF with about 400,000 new cases diagnosed each year [6,7].

The best clinical index to assess ventricular function, or lack thereof, is left ventricular ejection fraction (LVEF). LVEF is measured using the following equation:

$$\text{LVEF} = \frac{[\text{Ejected Stroke Volume (SV)}]}{[\text{End-Diastolic Volume (EDV)}]}$$

Equation 1

where the ejected stroke volume is the difference between the end diastolic volume and the end systolic volume. The table below shows how ventricular systolic dysfunction, one manifestation of CHF, affects volumes, pressure and heart rate.

Table 1: Comparison of Normal vs. Ventricular Systolic Dysfunction

	Normal	Systolic Dysfunction
End diastolic volume (ml/m ²)	80	135
End systolic volume (ml/m ²)	40	105
Stroke volume (ml/m ²)	40	30
Ejection fraction (%)	50-65	15-20
End diastolic pressure (mmHg)	10	25
Heart rate (bpm)	70	120

From the table, it is evident that although EDV, ESV and end systolic pressure increase in patients with CHF, stroke volume, the volume of blood ejected by the heart, decreases. This decrease is reflected in the ejection fraction which is well below the normal values. To compensate for the decrease in stroke volume, the heart beats faster, which leads to further enlarging of the LV.

3.3 Need/Market Analysis

Usually drug therapy and lifestyle changes are used to treat CHF. One treatment involves delivery of cell/gene therapy to the myocardium of the LV, thereby improving and restoring LV function. To accomplish delivery of the gene, a catheter is inserted into the femoral artery up to the aorta, and through the aortic valve into the LV.

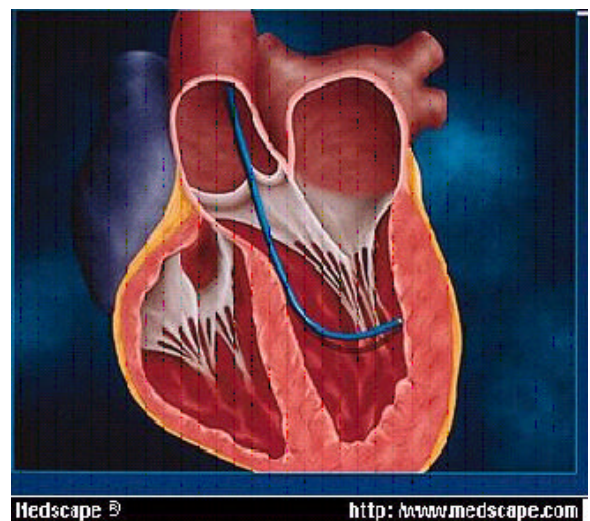


Figure 2: Catheter Navigation. This figure shows a schematic of a guiding catheter entering from the aorta into the LV.

Figure 2 shows a schematic of a catheter entering the LV via the aorta and articulating with the myocardium of the ventricle wall.

Testing and validation of this catheter system is important prior to clinical delivery of gene therapy medication. Testing will provide physicians critical parameters, such as length of time required for catheter to reach the left ventricle from the femoral artery and the exact path it must follow. It will also yield the optimal location in the ventricle to target as well as impact pressures caused by the catheter pressing against the ventricle wall. Validation of these variables will ensure success of interventional treatment.

Conventional testing of catheters is currently performed in animal models. There are several shortcomings to these models. First of all, a large number of ethical issues are associated with animal testing, especially in relatively early stages of testing and validation. Additionally, the animal model does not incorporate the difficulty of navigating a catheter through a normal beating heart, since heavy sedation of the animals alters the motions seen in the heart. There are also significant differences in terms of anatomical and physiological feature in animals as well as humans. Finally, animal models may not be suffering from congestive heart failure and thus the model is not fully realistic.

Thus, the need for a preclinical research model for intraventricular therapy is evident. Our model of the left ventricle will overcome many of the shortcomings in current testing and validation methods and will allow for Guidant catheters to successfully deliver gene therapy to treat congestive heart failure.

Our completed model will also serve as a method for studying pulsatile physiological flow in the descending aorta and downstream vascular tree of a human. This research will provide a deeper understanding of *in vivo* fluid mechanics. Knowledge of mechanical factors involved in blood flow can help prevent, diagnose and treat vascular disease as well as help in medical and surgical planning.

3.4 Benchmarking and Related Technology

Performing benchmarking activities and looking at related technologies for this project helped generate ideas that could be modified and incorporated into our design and also helped define the essential components necessary for our flow system. These components include a closed loop flow system capable of producing pulsatile flow and a deformable membrane.

3.4.1 Patent Summary

Reviewing current patents and technologies on the market helped reveal design ideas with features adaptable to our project (Appendix 7.4). One of the most important features of the CHF model being developed is the pumping mechanism. The pumping mechanism is crucial in both replicating the motion of a beating heart and creating a flow profile similar to that observed in the cardiovascular system. A variety

of pulsatile flow systems currently exist that allow the user flexibility in adjusting the flow characteristics. In addition, some devices allow the incorporation of medical devices such as ventricle assist devices and mechanical heart valves.

Understanding the temporal distribution of the electrophysiological pathways in the heart could provide valuable insight into the correct protocols to employ in driving our pumping mechanism. Many computer simulated heart models animate the conduction of depolarization wave patterns and reveal the interaction of multiple tissue groups in the heart. These tools could help in understanding how the action of different tissue groups could be represented in a physical model of the ventricle, whose motion is governed by pressure gradients versus muscle action.

3.4.2 Related Technology

The relevant technologies researched concern the different types of pulsatile pumping mechanisms available and the materials most appropriate for creating a deformable membrane.

Pulsatile Pumping Mechanism: The first type of pumping mechanism involves a piston actuator that is displaced along its central axis to generate positive and negative pressures. An example of this, the Harvard Pulsatile Pump, is shown in Figure 3. The piston consistently travels to the end of the ejection stroke, which causes the pump to completely empty at each cycle. Flows are regulated by ball check valves inserted at the piston heads. The pulsatile output of the piston actuator mechanism aims at replicating the pressure and flows seen *in vivo* in the ventricles of the heart. Another pumping mechanism employs a pneumatic pump and compression chambers. A control circuit regulates the frequency and pressure of blasts of pulsed air that are applied to a fluid column. The control circuit contains high speed on/off switches that selectively supply or deprive the fluid column with pressurized operating media. This creates either positive or negative pressure that cause the piston to be displaced in either the positive or negative direction along its central axis.



Figure 3: Harvard Pulsatile Pump. The pulsatile pumping mechanism consists of a piston actuator and ball check valves. These components aim at reproducing physiological flow conditions.

Deformable Membrane: Looking at technologies used in making deformable membranes essentially entailed researching materials with the appropriate viscoelastic properties. Our findings showed silicone, urethane, and polyvinyl alcohol (PVA) to be the first possible candidates. Silicone is relatively sturdy, however under sustained use, the material weakens and is prone to tearing. Urethane is translucent when used to create a smooth, thin layer; however, increasing thickness and introducing geometrical complexities makes this material more rigid and opaque. It provides considerable strength relative to the other materials. PVA is an extremely clear and flexible material. Although initially an attractive candidates, PVA tears easily and must be submerged in water at all times.

Existing Models: Since designing a clinically realistic model of the left ventricle is such a specialized design problem, few products already exist that accomplish this task. However, one group at Ghent University in Belgium actually fabricated a model very similar to the one envisioned by our design team. Figure 4 [2], illustrates the design features and opportunities of this model. The model was described in the following manner:

“Physical true scale model of the left heart. The contraction of the elastic atrium and ventricle is realized by means of pressurized air. The electronic part allows the independent regulation and monitoring of left atrial and ventricular pressures and volumes. Atrial and ventricular pressure and volume, mitral flow and aortic flow are continuously measured. The flow field through the mitral and aortic valve can be visualized by color echo-Doppler (Vingmed CFM 800). The model can be used for calibration and testing of medical devices (vibrocardiography, color echo-Doppler,..), for testing of artificial heart valves, verification of mathematical models...”



Figure 4: Pulse Duplicator System. Designed at Ghent University in Belgium, this model of the left heart incorporates a pressurized air system to regulate and monitor flow through the mitral and aortic valves.

3.5 Problem/Needs Statement

Congestive heart failure (CHF) is a fatal syndrome that captures many lives every year. Guidant Corporation has a catheter based method of delivering cell gene therapy to treat the thinning walls of the left ventricle. In order to test and validate their system, they require a visible dynamic model of a left ventricle that mimics the anatomy and flow profile of a human heart.

Our objective is to design a clinically realistic model of the CHF left ventricle that satisfies specific engineering requirements. This model will also be used to study flow in the descending aorta and vascular system in terms of mechanical properties. Our final deliverables will include a full flow system consisting of a pumping mechanism and a dynamic ventricle. We will also prepare a final report and presentation.

3.6 Project Team

The three team members working on this project are Ayodope Anise, Stephen Meier and Sonar Shah. The following paragraphs present a short background on each of the members.



Ayodope is currently pursuing a Master's Degree in Biomechanical Engineering with a focus in Medical Device Design and Cardiovascular Biomechanics. Upon completion of her degree Ayodope hopes to gain experience in the medical device industry, particularly device design, prior to pursuing a degree in Medicine.

In May 2001, Ayodope obtained her Bachelor's Degree in Biomedical Engineering, with a focus in biotechnology, from Yale University. In addition to her undergraduate coursework, she spent a summer completing a Medical Biology Course at the University of Pittsburgh Medical School. The course included viewing of cadavers and clinical pathology conferences, allowing for hands-on exposure to various disease states. More recently Ayodope was employed as a clinical engineer for the University of Pittsburgh Medical Center's Artificial Heart Program. Here she obtained knowledge of and training with heart assist devices including the Intra Aorta Balloon Pump (IABP) and Ventricular Assist Devices (VADs).



Stephen is currently pursuing a Master's Degree in Biomechanical Engineering. He is concentrating on Medical Device Design and overall Product Development for Marketing and Manufacturing. After completion of his degree, Stephen hopes to enter the medical device industry as a project engineer.

In June 2001, Stephen obtained his Bachelor's Degree in Biomedical Engineering, with a focus in Biomechanics. His coursework showed him the fundamental theories behind engineering practice, the research techniques to qualitatively and quantitatively test these theories, and the appropriate design methodologies to employ in developing mechanical systems. Under the Cooperative Engineering Program, he spent nine months working as a research engineer for Depuy Orthopaedics in Warsaw, Indiana. Working in the Mechanical Testing Division gave him a large insight into the failure modes of various orthopaedic implants. It also equipped him with 3-D modeling tools, appropriate testing procedures, and data analysis techniques to analyze the different modes of failure.



Sonar is currently pursuing a Master's degree in Chemical Engineering with a strong focus in Biomedical Engineering. She is presently working on a computational project under Dr. Charles Taylor involving the analysis of factors that promote blood clot formation and thrombosis in arteries. Upon completion, Sonar wishes to work in industry, as an engineer, in the field of biomedicine.

In June 2001, Sonar obtained her Bachelor's degree in Chemical Engineering from McGill University. Her undergraduate course work has provided her with a strong theoretical background about the principles of engineering and design. She also spent a summer term working at the University of Calgary on a biomedical research project analyzing rabbit bones using CT scanners to determine their porosity and the onset of osteoporosis. Additionally, she has done some design work with clients from industry. One of the projects, from Hatch Inc., dealt with the design of a ferrochrome production plant. She feels the skills of planning and evaluating that she has developed will be of benefit when working on the Guidant project.

3.6.1 Project Sponsor Contacts

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4.1 Purpose of Design/Model

Our model will enable preclinical testing of catheters used to deliver gene therapy to the myocardium weakened by CHF. Current methods used to test catheter system employ static models of the heart and do not capture many of the complexities involved in a dynamic model. Catheter maneuverability can only be approximated in static ventricle models, since the effects of wall motion are not taken into account. Our model will enable the operator to evaluate the accuracy to which they can target an area of the heart for drug/gene therapy. Introducing wall motion better represents *in vivo* conditions and informs the user of the reproducibility of the catheter systems.

A clinically realistic model for CHF will also allow for modeling of flow through the aorta, thereby contributing to a better understanding of *in vivo* fluid mechanics. Our completed model will serve as a method for studying pulsatile physiological flow in the descending aorta and downstream vascular tree of a human. When compared to physiological data, a physical model can provide a quick, accurate, and cost efficient means of validating numerical models of the vascular system. Improved models lead to increased knowledge of the mechanical factors involved in blood flow and can help prevent, diagnose and treat vascular disease, as well as aid in medical and surgical planning.

4.2 Project Goals

In order to develop a clinically realistic CHF model, the project has four main goals:

- ?? Design a closed loop pulsatile flow system that incorporates a model of the ventricle in the form a deformable membrane
- ?? Prototype and validate system
- ?? Optimize system to meet design requirements
- ?? Finalize and document the design specifications, fabrication techniques, and testing and operational procedures

The team must develop a design that dynamically simulates the motion of the left ventricle (LV) of a patient suffering from Congestive Heart Failure (CHF). This design must incorporate a pulsatile flow system that represents the fluid mechanics of blood flow in the body. The pulsatile system will be driven by changes in pressure in a central chamber, which cause the successive expansion and relaxation of a deformable membrane model of the left ventricle. Expansion of the membrane will

draw in the blood analog, while relaxation will cause ejection of the blood analog in volumes comparable to *in vivo* ejection volumes. The prototyped design concept should serve as a “proof-of-concept” that validates the proposed mechanisms just discussed. Further work with the prototype will optimize the flows and pressures seen, to ensure that the final device fulfills the design requirements. In the final stages of the project, the exact design specifications, fabrication techniques, and testing and operational procedures will be documented to ensure the sustained functioning and reproducibility of the device.

4.3 Scope of the Project

We will design and construct a prototype of a clinically realistic model for CHF. It will allow for testing of catheter-based drug/gene delivery systems, in addition to providing a better understanding of *in vivo* fluid mechanics. The model will be optimized and tested to ensure close approximations to *in vivo* conditions. The project will not focus on manipulating Guidant’s current model of CHF LV geometry, but rather incorporate the current geometry into the prototyped flow system. In addition, the pumping mechanism used will be a standard Harvard pulsatile pump, in which only minor manipulations will be made to ensure the correct flows. Efforts will not be concentrated on redesigning the pumping mechanism, but rather in integrating the pumping mechanism into the desired flow setup.

4.4 Functional and Physical Requirements

Table 2: Weighting of Functional Requirements

Functional Requirements	Criteria Weighting (1-20)
Pulsatile flow	20
Ability to directly visualize the catheter system	20
LV wall motion (5.8-7.0 cm change in short-axis/8.8-10.0 cm change in long-axis)	17
Adjustable heart rate (70-120 bpm)	17
Blood analog perfused at body temperature (37°C)	12
Adjustable LV ejection fraction (15%-40%)	12
Pressures comparable to internal human systolic/diastolic pressures (120/80 mmHg)	8

Table 3: Weighting of Physical Requirements

Physical Requirements	
CHF LV geometry	20
Heart valves (synthetic/tissue) that enable catheter access across it into LV	20
Femoral access to the LV via the aorta	14
Chamber capable of accommodating a worst case dilated CHF LV (9.0 cm short-axis, 12.4 cm long-axis)	12
Fluoroscope compatibility	12
MR compatibility	8
Internal surface texture	8

The functional and physical requirements are listed in the table above, with criteria weighting assigned to each requirement. The criteria weighting rates the importance of each requirement in the eyes of the Guidant team from both a functional point of view and from the feedback we have received from our campus and corporate sponsors. As you can see, the three most important functional requirements include pulsatile flow, the ability to directly visualize the catheter system, and LV wall motion. The top three physical requirements include CHF LV geometry, incorporation of heart valves, and femoral access to the LV via the aorta. Requirements that fall lower within the rankings are those that are desirable for the final system; however, they are not crucial for a fully functional device.

4.5 Regulatory Considerations

The CHF model, most likely, falls outside the definition of a medical device. Its only implication in FDA regulation would be if measurements taken from the model were used to validate other FDA regulated medical devices. Thus, the purpose of the model highly determines whether the model is subject to FDA regulations. If, for example, pressure measurements at the wall are taken during simulated gene therapy and used for verifying the safety and effectiveness of new catheter systems, Guidant would need to substantiate the extent to which the CHF model accurately represents *in vivo* conditions. High pressures may pose a safety risk to the patient, and the ability of the model to measure these pressures would need to be demonstrated.

5.1 Vision/Strategy

The vision of the Guidant Design Team is to design and complete a flow system that incorporates a deformable left ventricle and Guidant's vascular model of the aorta through the femoral arteries. This vision will be accomplished through early prototyping, regular meetings with members of Guidant Corporation and Stanford mentors to review design options and milestones, and through continued open communication among members of the design team.

5.2 Overview of Work Completed

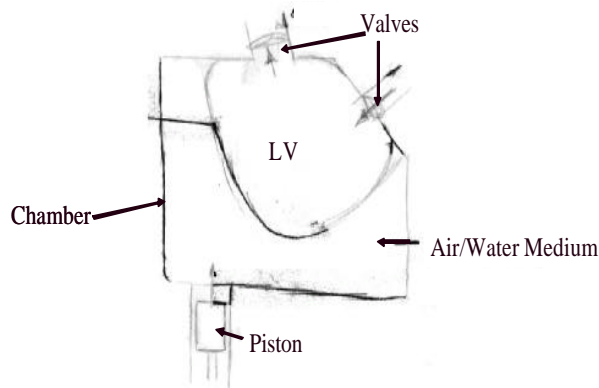
During the winter quarter, our team was successful in generating several preliminary design ideas, choosing a single design concept, and creating an initial prototype. Prior to midterm we presented five design ideas and from there chose the two most feasible designs. After further consideration, discussions with our corporate sponsors and our on-campus advisors, we chose a single design and began the process of producing a working prototype. This process is expanded upon below.

Our current path has included purchase of all necessary materials for an initial prototype, prototypes of our flow system and chamber, and prototypes of the deformable ventricle. In addition, we have mixed samples of several materials that we are considering for the final model of the left ventricle and created CAD models that will be used next quarter for final prototyping.

5.3 Design Concepts Generated

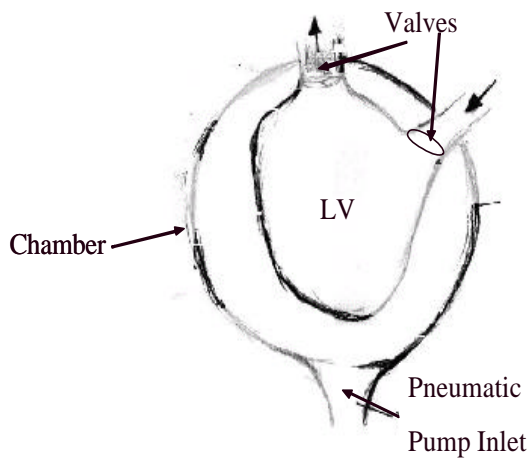
Below are five preliminary designs that were completed early in the term.

5.3.1 Single Piston



The Single Piston mechanism consists of a chamber filled with either an air or water medium. It is driven by a piston that produces positive pressure causing the LV to collapse. This design allows the LV and catheter to be viewed, and the piston allows for an adjustable heart rate. In addition, two valves will be incorporated into the model to simulate the aortic and mitral valves. One challenge in this design is ensuring that the ventricle is tightly sealed in the chamber and there is no leakage of fluid.

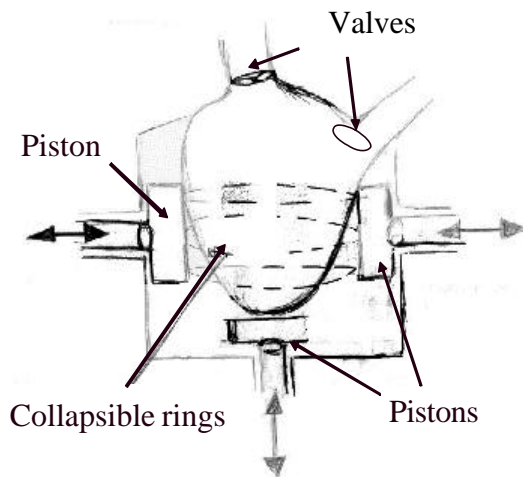
5.3.2 Pneumatic Pump Mechanism



This design uses a pneumatic pump to provide a vacuum or negative pressure that would cause the LV to contract and also provide positive pressure, thereby enabling the ventricle to return to its relaxed state. The chamber could be a cube or a sphere, as a cubical chamber allows for ease of manufacturability. In addition, a ventricle in the systolic (contracted) state was considered. The vacuum could be used to stretch the ventricle and increase its volume. Alternatively, the ventricle could be fabricated midway between systole and diastole to reduce the amount of stretching

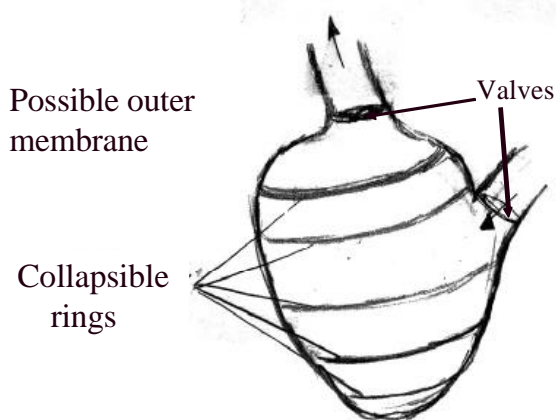
necessary to obtain sufficient volume. This design also incorporates valves and allows for a maximal viewing surface. The challenge of this design would be to ensure the exact specifications of the ventricle.

5.3.3 Multiple Piston Mechanism



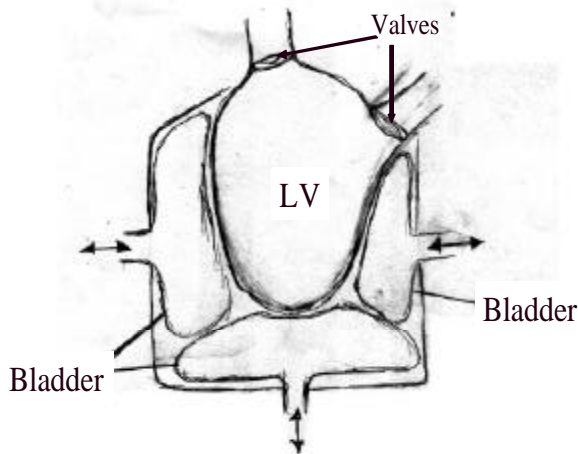
This mechanism uses several pistons that act directly on the LV to cause its contraction. By using several angled pistons, one can better mimic the non-uniform contraction of the ventricle. One additional modification of this design would be to attach rings to the piston to aid in returning the ventricle to its original state. Again, valves are labeled in the diagram to show where the aortic and mitral valves will be placed. One major shortfall of this design is that it would definitely reduce the viewable area of the ventricle. In addition, the multiple pistons make this design more difficult to prototype.

5.3.4 Collapsible Rings



The design shown at left would use rings to collapse the LV. An outer membrane would surround the ventricle and reduce any damage produced by the rings if they were in direct contact with the ventricle. This design, like the others, includes two valves. Problems with this design include the following: determining a method for controlling the rings, either electrically or mechanically, and lack of visibility if the rings are made of metal. If the rings are clear plastic then there may be problems with their durability. Also, during the contraction phase, there may be a problem of material bulging in the areas between the rings.

5.3.5 Multiple Bladders



The Multiple Bladder design would use transparent or translucent bladders, which would be filled with water or air, to collapse the ventricle. By using several bladders and compartmentalizing them, one could better mimic the non-uniform contraction of the ventricle. However, regulating the pressure produced by each bladder may be difficult. As well, if the ventricles were not made to fit the shape of the ventricle, they may not create the contraction desired. They may also stick to the ventricle during the relaxation phase. Additionally, if the

bladders are not clear they will impede visibility.

During a meeting with our corporate sponsor we reviewed the above designs and reduced the options to designs one and two. As stated in the above analyses, these designs achieved the specified requirements and simultaneously enabled a relative ease of manufacturability. A formal Pugh analysis was not completed for designs three through five; however, through discussions of these designs it was determined that the possible problems and shortfalls, given in the summaries above, were too great to overcome. In addition all three designs fell short of major design requirements such as visualization of the catheter.

5.4 Evaluation of Designs

After further consideration, design one, the Piston Mechanism, was chosen for initial prototyping. The Pugh Chart below shows the criteria that were considered during analysis of our two final design concepts. The criteria weighting, given on a scale of 1-20 conveys the importance or necessity of a design requirement with a value of 20 denoting most important.

Table 4: Pugh Chart

Design Requirements	Criteria weighting	Design Concepts	
		Piston	Pneumatic Pump
Pulsatile flow	20	10	6
CHF LV geometry	20	10	10
Ability to directly visualize the catheter system	20	9	9
Heart valves (synthetic/tissue) that enable catheter access across it into LV	20	10	10
LV wall motion (5.8-7.0 cm short-axis/8.8-10.0 cm long-axis)	17	10	10
Adjustable heart rate (70-120 bpm)	17	10	6
Femoral access to the LV via the aorta	14	9	9
Blood analog perfused at body temperature (37°C)	12	10	7
Chamber capable of accommodating a worst case dilated CHF LV (9.0 cm short-axis, 12.4 cm long-axis)	12	9	9
Fluoroscope compatibility	12	9	8
Adjustable LV ejection fraction (15%-40%)	12	9	8
MR compatibility	8	8	8
Internal surface texture	8	8	8
Pressures comparable to internal human systolic/diastolic pressures (120/80 mmHg)	8	8	6
Weight		0.94	0.53

A Pugh chart is a method of evaluating the different design concepts with regards to the extent which they fulfill the design requirements. A Pugh chart was done for the pneumatic pump and the piston mechanism, as they were the two concepts that seemed the most feasible.

The pneumatic pump was given a lower rank for its ability to provide pulsatile flow. The reason behind this is that the pump itself must contain two systems, a vacuum system as well as a pressure system, in order to operate. The vacuum system imposes a negative pressure in the chamber and causes the ventricle to expand. An automated check valve is then used to switch over to the pressure system causing the ventricle to then return to its original contracted conformation. The use of two system at the pump inlet, as well as the control of the automated check valve, complicate the mechanism greatly and reduce the ability to provide pulsatile flow. The pneumatic system is also ranked lower for adjustable heart rate for the same reason as mentioned above.

Perfusing a blood analog at body temperature (37°C) is more difficult in the pneumatic system because we will require two different heating methods, one for the air medium in the chamber and one for the water in the left ventricle. This will provide more of a challenge than the piston mechanism, which only requires heating one medium, water, for the entire system to be at body temperature.

The mechanisms also differ in terms of creating physiological pressures within the ventricle. It is more difficult in the pneumatic system because air is a compressible fluid, and thus, creating such high pressures will be a challenge.

The two mechanisms are comparable in terms of allowing for CHF geometry in the left ventricle, ensuring visualization of the catheter, incorporation of tissue valves in the ventricle, as well as LV wall motion. These criteria do not affect either pumping mechanism in any way.

The two mechanisms are also comparable in terms of access from the femoral artery through the aorta into the left ventricle, fluoroscope compatibility, MRI compatibility, and internal surface texture.

From the Pugh chart, it is evident that the piston mechanism comes out above the pneumatic mechanism in terms of meeting the requirements. The piston method was chosen for this reason for further prototyping.

5.5 First Prototype of Design

As stated previously, our group successfully completed an initial prototype. The prototype, shown below in Figure 5, consists of a chamber that incorporates a deformable left ventricle and a flow system that provides pulsatile flow. Some key features of the flow system are the chamber, the outflow reservoir, the supply reservoir, and the Harvard Pump.

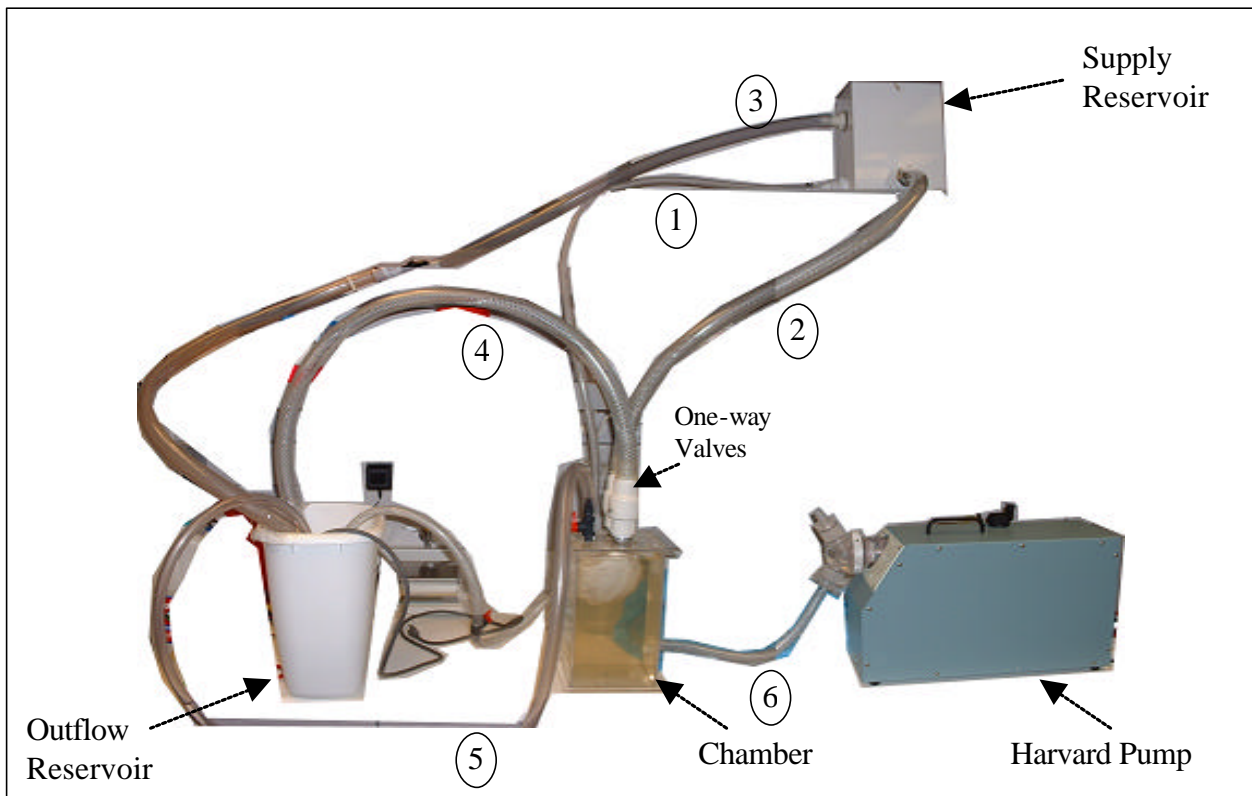


Figure 5: Prototyped Flow System. This closed loop flow system incorporates a piston actuator that creates positive and negative pressure in the clear plastic chamber. These pressures cause a deformable membrane model of the left ventricle to relax and expand in a pulsatile manner.

The flow of water can be seen by the streams that are numbered. Flow 1 is from the outflow to the supply reservoir and is driven by a fish tank pump submerged in the outflow reservoir. Flow 2 is from the supply reservoir to the left ventricle through the mitral valve. It is driven by the expansion of the ventricle caused by the negative pressure created in the chamber. The negative pressure is a result of flow 6 which is the motion of the actuating piston within the Harvard pump. Flow 3 is from the bleed valve of the supply reservoir to the outflow. It ensure that there is a constant head, or height of water, in the supply reservoir, thereby providing a constant hydrostatic pressure. Flow number 4 is from the ventricle through the aortic valve to the outflow reservoir. This flow is pulsatile and the ejection volumes are controlled so they meet the design requirements. Flow 5 is from the release valve of the chamber. This is only important initially when filling the chamber to ensure that it is completely air tight.

5.5.1 Chamber

The Chamber of our flow system, Figure 6, was constructed from a 3/16 inch acrylic sheet. A two dimensional CAD file was created and the acrylic sheet was cut to the specified dimensions using the PRL Lasercamm. Screw holes were tapped using holes cut by the Lasercamm, and the base of the chamber was then assembled using silicon glue. Next, adapters, which would be used to connect unidirectional flow valves and tubing to the chamber, were attached. A sealant was used to improve the seal around all valves and adapters. The final chamber included two spring loaded unidirectional flow valves, a release valve that was used to fill the the chamber with fluid, and a threaded connection to which tubing was connected to incorporate the Harvard Pump.



Figure 6: Chamber Prototype. This clear, acrylic chamber encloses the deformable ventricle model and is pressurized during flow.

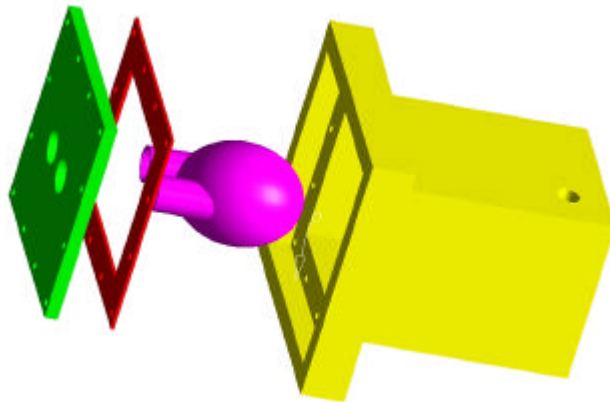


Figure 7: Redesigned Chamber. This CAD image illustrate the chamber modifications necessary for next quarter. The new chamber should incorporate a removable top and gasket for sealing purposes.

When we prepared for testing of the flow system, the ventricle was attached to the unidirectional flow valves, via male-male adapters, using plastic tie clamps. Finally, the lid was sealed to the base, again using silicon glue. One may notice that the base of the chamber is significantly longer than the length of the LV. This was done to ensure that a uniform increase in pressure within the chamber, not the turbulence produced by the bolus of water injected, caused deformation of the ventricle. After completion of our initial prototype, a few design changes were made. These changes are illustrated in Figure 7. The CAD image shows a flange that will be attached to the base of the chamber to provide support and improved attachment of the lid. A rubber gasket, shown in red, will be used to mate the base and lid of the chamber and provide a fluid tight interaction. Screw holes and screws will be placed in the lid, through the gasket, and into the flange to join all three pieces and allow for repeated attachment and removal of the lid. This was not possible in our initial prototype. Holes, approximately one inch in diameter, will be placed in the lid to allow for attachment of the LV and inflow and outflow tubing. Additionally, a half inch diameter hole will be placed near the base of the chamber to allow for connection to the Harvard Pump.

Next quarter, upon completion of the final CAD image (i.e. incorporation of holes for release valve and pressure gauge), the manufacturing of the chamber will be outsourced to a machine shop.

5.5.2 Supply and Outflow Reservoir

The outflow reservoir supplies water, via a release valve on the lid of the chamber, during initial filling of the chamber. The outflow reservoir also provides water to the supply reservoir to sustain a constant volume of water, thereby maintaining a constant pressure head. A fish tank pump is used to pump water to the chamber during initial filling as well as to the supply reservoir when the flow system is running.

The supply reservoir provides flow to the LV. Near the top of the supply reservoir is an overflow valve which allows excess water to return to the outflow reservoir, thereby helping to maintain a constant pressure head.

5.5.3 Harvard Apparatus Pulsatile Blood Pump

The Harvard Pump is a piston driven pulsatile pump that is capable of delivering human physiologic flow rates and pressures in waveforms similar to those produced by the heart [3]. The pump maintains the required heart rate of 70-120 beats per minute and the cycling of the piston provides the pressure necessary to cause contraction and deformation of the LV.

5.5.4 Left Ventricle

To quickly obtain a LV prototype that could be incorporated into our flow system and that allowed for pulsatile flow, simple methods of development were used. One method was to coat a balloon with latex, thereby creating a more rigid, but deformable surface, similar in shape and size to our desired final product. Figure 8 shows the model that was completed in this manner and was successfully incorporated into the flow system.



Figure 8: Latex Balloon. This latex balloon represents one of our initial ventricle prototypes

A second method that was used to create a deformable LV ventricle is illustrated below in Figure 9. For this prototype a Stereolithography (SLA) model (9a) and a sample of urethane were obtained from Guidant Corporation. The SLA was coated with urethane, as seen in figure 9b, and after curing for 24 hours, a deformable ventricle was obtained (9c). One of the major problems with this method of prototyping is the difficulty of obtaining a uniform thickness when coating the SLA. In addition, to remove the prototype from the SLA, the urethane must be cut and reattached using

glue. The seam that forms when the ventricle is glued may be an area of leakage or failure in the model. It is also unknown how the glue will affect deformation of the ventricle

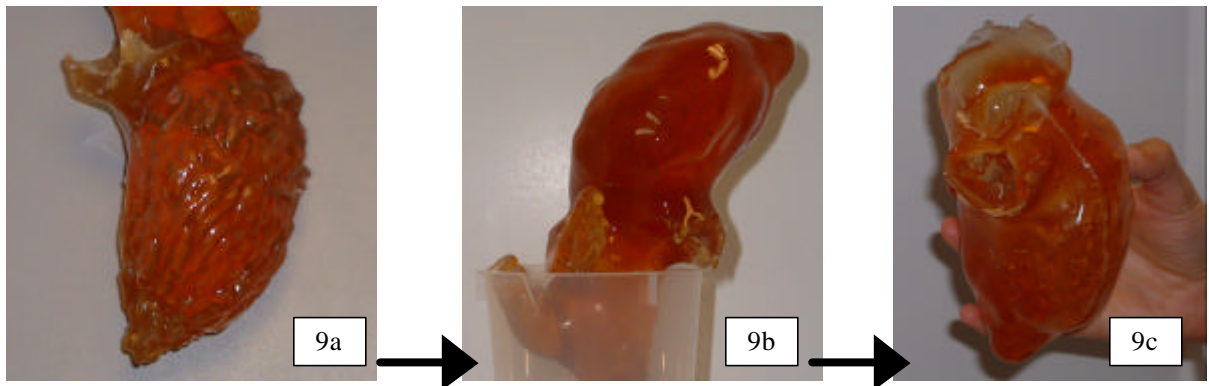


Figure 9: LV Formation. This flow chart outline the steps involved in creating a deformable LV membrane. 9a shows the initial geometry used. In 9b, the urethane material is curing, which ultimately yields the model shown in 9c.

Another milestone in formation of a LV was modification of an IGES file obtained from Guidant Corporation. The steps that were completed this quarter are illustrated below (Figure 10). The original IGES file had a fairly complicated surface geometry that was simplified significantly. Also, the size of the ventricle was reduced and the atrium removed, since our project does not include that portion of the heart. Next, a box was created to surround the model, and the model was subtracted from the interior. Next quarter, we may use this design to create a Fuse Deposition Model (FDM) that can be used produce a negative of the model. This negatives can produce multiple positives, which can then be coated with various materials to obtain prototypes of our LV.

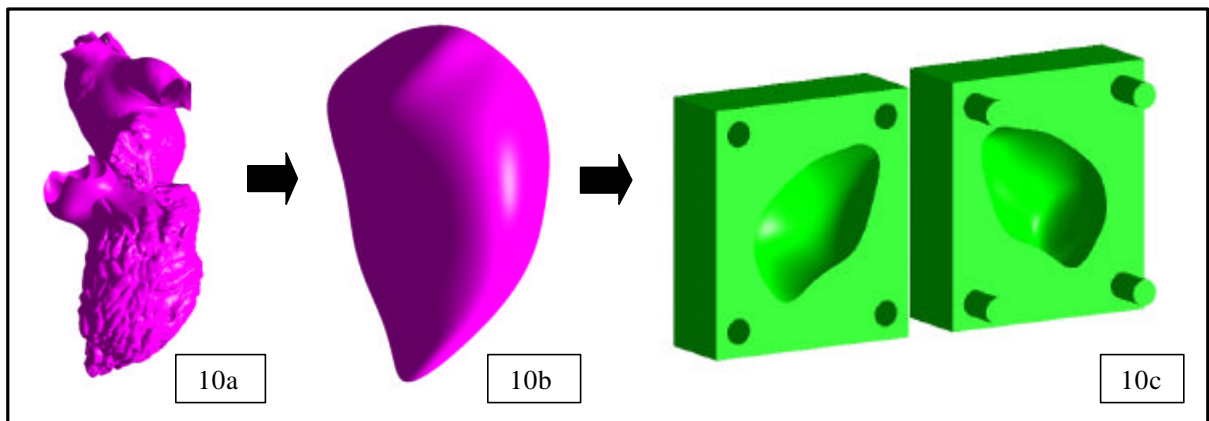


Figure 10: Modification of IGES File. The initial IGES file contained a large number of complex surfaces (10a). These surfaces were simplified to form the model shown in 10b. Next, a box with the subtracted model yield a negative molding tool.

6.1 Overview

This quarter was spent defining the scope and goals of the problem, determining the specific engineering requirements the design must fulfill, brainstorming and evaluating design concepts, as well as gathering materials to build our first prototype. By the end of the quarter, our flow system was set up and tested. Based on our accomplishments this quarter, the challenges we have faced in the operation of our initial flow system, we have developed a timeline that includes specific goals for spring quarter.

6.2 Deliverables

The final deliverables for our project will include a completed flow system that incorporates a deformable LV, mimicking changes in the short and long axis of a patient suffering from congestive heart failure. It will also accommodate the attachment of Guidant's vascular model, consisting of the aorta down to the femoral arteries. The model will allow for visualization of a catheter in the ventricle and will operate close to body temperature. Pressure and temperature sensors will enable specific parameters to be measured throughout the system.

We will also deliver a report of testing and evaluation results of our final flow system, along with the final report and presentation.

6.3 Methodology

Our initial ideas for materials to use for the ventricle, as well as for the creation of a pumping mechanism, came from our conversations with our sponsor and mentors. Our own personal background experiences also contributed. Research was done on previous work similar to our project, in addition to looking at available patents. These patents gave us a better understanding of the feasibility of our ideas. Our ideas were then refined and modified according to ease of manufacturability and the extent to which each idea fulfilled the design requirements. The design ideas were visualized in more detail both by physically setting them up and creating drawings in CAD programs such as Unigraphics and AutoCAD.

The construction of our initial prototype began with chamber fabrication in the Stanford Product Realization Lab (PRL). Our initial flow system prototype and ventricle fabrication was set up in Dr. Taylor's lab. Materials were purchased from Home Depot, McMaster Carr, as well as provided by Guidant and Taylor's lab. For

next quarter, our fabrication, set up and evaluation will continue. Portions of our project, such as chamber development, will be outsourced.

6.4 Reliability and Validation

The prototype we have created will be tested and modified in a number of ways. By filling the system with water and turning on the Harvard pump, we can see the deformation of the ventricle qualitatively and calculate its deformation quantitatively by measuring the ejection volume. Also, the strength of the chamber seals and attachment of tissue valves and ventricle to the chamber can be noted. Modifications can be made based on the observation of running the flow system.

Finite element analysis will also be very valuable in this area of the project. It will give us the deformation of the ventricle for a variety of pressure differences and material properties. By using this information, we can simulate design iterations using a computer model. This will indicate the appropriate wall thickness necessary to produce the desired deformation. This method will save us time by not having to experiment with numerous ventricle prototypes.

The final system will be validated in terms of adjustable heart rate, adjustable ejection volume, as well as how well the model represents human anatomy and physiology in terms of structure, pressure, temperature and most importantly, flow pulsatility.

6.5 Major hurdles

One of the difficulties the Guidant team faced was choosing a material for prototyping the ventricle. Some of the design constraints on the material were visibility, strength and minimal adhesion to other materials. The three materials in consideration were silicone, urethane and PVA. Despite the attractive properties of PVA, it was eliminated during the early design stages because of its lack of strength. Silicone was considered for some time as Sylgard 184, a particular type of silicone, was shown to be less adhesive than other forms. Its strength is still questionable and thus will most likely not be used. Molds of sylgard were still created for testing of material properties. Urethane, although not completely clear, is fairly translucent when it is thin and is durable enough to withstand numerous cycles of expansion and contraction. One of our prototypes was created out of urethane to get a qualitative feel of its strength.

The group overcame a major hurdle when dealing with the IGES file. In this 3D CAD file provided to us by Guidant, the original part was scanned and the resulting point cloud was surfaced to obtain a realistic representation of the left chamber of the heart. The initial file contained more than 1100 surfaces on the left ventricle and also contained unnecessary parts such as the atrium and aorta. Converting this file into a format in Unigraphics that we could manipulate was extremely challenging, as the package could not recognize the individual surfaces as a unified solid. In order to deal

with this difficulty, Guidant provided a simplified model. The LV approximation did not contain as many trabeculated surfaces and was uniformly scaled down to meet systolic volume measurements. The file was then used to create drawings of negative molds, which will further be used for ventricle prototyping next quarter.

Another challenge the team faced was creating a secure seal on the chamber. It is very important that the system does not leak, because not only will water spill everywhere, but it will reduce the pressure in the chamber created by the Harvard pump, and the deformations and ejection volumes of the ventricle may not be as desired. Liquid glue specifically for acrylic plastic was used to seal the edges; however, because we wanted to reuse the chamber for the testing of multiple prototypes, the top was sealed with a silicone kitchen and bath formula. This seal did not provide the required strength, and leakage was observed. One solution to the problem is to use more sealant, or a different type of sealant.

Fastening the ventricle to the chamber was another area of difficulty. Since a latex-coated balloon was used as our first prototype, holes were created for attachment of the balloon to adapters that were connected to unidirectional flow valves. The holes were placed over the adapters and secured with plastic ties. This was shown to not be as secure as anticipated, since the balloon ventricle started to slip off the adapters after our first test. Our next prototype will be designed differently to avoid this problem. One change will be that the ventricle will have two tubes protruding out of it. This will provide extra material for fastening and will ensure that the attachment of the ventricle to the valves and chamber is more secure.

6.6 Foreseen Challenges

6.6.1 Attaching the tissue valves to the system

Because the tissue valves have not been obtained yet, it is difficult to approximate what size we will receive, as well as the size of opening in the ventricle we should create to incorporate the valves. Also, the valves will be fixed and will come inside a ring. Our possible attachment options include suturing, gluing or fastening with a flange.

6.6.2 Formation of final LV with varied wall thickness

This was also a problem we faced this quarter when forming our prototypes. When creating both the latex balloon prototype and the urethane coated SLA prototype, the thickness was very random and depended on how the material was painted on, or how far it dripped before it dried. We hope the finite element analysis will determine what exact thickness we are looking for in each area. We then hope to incorporate the results into our mold design.

6.6.3 Competing wall thickness requirements

Our final ventricle must be thin enough to allow for visualization, especially with the urethane material, as well as to allow for the appropriate amount of deformation. We found that the latex balloon did not deform as much as we would have liked because it was quite thick. However, we must ensure that the model is not too thin because it should not tear or collapse in any location, even after numerous cycles of pumping.

6.6.4 Integrating the LV into the chamber

We have not finalized the exact method of fastening the left ventricle into the chamber. One method is to attach it exactly where the valves are located. Another option is to attach it slightly below the valves, so the valves will be outside of the chamber. Both methods will have to be tested to see where the strongest bond can be made.

6.6.5 Attachment of vascular model to the final system

The vascular model, consisting of the aorta to the femoral arteries (provided by Guidant), must be attached to our chamber at the location of the aortic valve. Because this model cannot be stretched or deformed when it is fastened, we may have to modify the top of our chamber so it is slanted to accommodate the model at an angle.

6.7 *Timeline*

The Guidant team is pleased with the amount of work we have accomplished during the first quarter. The initial phases of the project consisted of a detailed tour of Guidant, including its research lab areas, as well as a meeting with the project mentor Dr. Chris Elkins and a tour of Dr. Taylor's lab. Shortly following the tours, the team brainstormed a variety of pumping mechanism that would enable the contraction and expansion of the ventricle. These ideas were reviewed by the class teaching team, our Stanford mentors, as well as our contact at Guidant to ensure each idea's feasibility. These ideas were then evaluated in more detail according to the essential and desirable design requirements, and one design option was selected for prototyping.

Prototyping, which began in mid-February, consisted of ventricle, chamber, and flow system construction. Weekly meetings with our sponsor, our Stanford mentors and the class teaching team ensured we were on track. In March, all of our work was combined to produce a working prototype. By evaluating the performance of our initial prototype, the group has a strong sense of areas that need to be improved and the timeline that must be followed for next quarter.

In April, the team will finalize the chamber specification and create detailed CAD drawings to outsource. While that is being completed, we will also spend a lot of time on finalizing the ventricle. Material testing will be done to determine which material

best fulfills our needs. As well, Finite Element Analysis will yield the thickness and pressures necessary to produce the desired deformation. By the end of April, we hope to combine the ventricle into the flow system and focus our attention of integration of the valves as well as other changes to optimize our flow system. Towards the middle of May, we hope to run a number of tests on the flow system and evaluate its performance in terms of its ability to meet the design requirements. This information will be included in our final report and presentation we will submit in June.

The Gantt chart in Appendix 7.8 presents our timeline in more detail with all of our tasks and subtasks outlined.

6.8 Individual responsibilities of team members

Each of the team members brought a unique set of skills and experiences to the project. In addition, each member was very enthusiastic to learn about areas in which they may have had minimal previous experience. All members were involved in the initial brainstorming sessions from which our design concepts stemmed. The presence of all the members was useful because we were able to bounce ideas off of one another, combine ideas, as well as eliminate ideas that were not feasible. All group members have also been present at all sponsor and mentor meetings.

After the midterm presentation and report, the project was broken down into more individual responsibilities. Steve worked a great deal with the CAD files and creating the negative molds out of the model provided by Guidant. He also took the initiative to meet with Chris Elkins to get feedback on how the flow system would be set up. Sonar also assisted in the final set up and operation of the flow system.

Sonar and Ayodope worked together to produce prototypes for the ventricles. Additionally, they received feedback from Mary Draney about materials and constructed molds at Guidant. These materials will further be used for material testing. Ayodope also worked with Alberto Figueroa to obtain information on non-linear elastic models to fit material data for FEA.

All three group members contributed to shopping for the supplies required for all the prototyping that was done this quarter. As well, everyone contributed to the final report and presentation.

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Personal Interviews

1. Mary Draney, multiple occasions
2. Chris Elkins, multiple occasions
3. Guidant sponsors, multiple occasions
4. David Parker, Feb 20 2001
5. Charley Taylor, multiple occasions

7.1 Presentation slides

Design of a Clinically-Realistic CHF Left Ventricle

Sponsored by *Guidant Corporation*

Ayodope Anise, Stephen Meier and Sonar Shah

March 11th, 2002

Overview

- Project Scope
- Motivation
- Initial Design Concepts
- Design Requirements
- Initial Prototyping
- Next Steps
- Foreseen Challenges
- Final Deliverables

Project Scope

- Develop, design and prototype a dynamic simulator of left ventricle (LV) of a patient suffering from Congestive Heart Failure (CHF)
- The design will be clinically realistic and meet specific engineering requirements

Motivation

- Congestive heart failure (CHF): the diagnosis given when the heart is unable to maintain adequate circulation of blood throughout the body due to circulatory congestion
- Affects more than 5 million Americans¹ and more than 22.5 million people worldwide²
- Fifty percent of patients diagnosed with CHF perish within 5 years³
- Drug therapy and lifestyle changes are common treatments for CHF

¹National Heart, Lung, and Blood Institute, National Institutes of Health, Data Fact Sheet

²New Medicine Report

³National Heart Lung and Blood Institute (NHLBI), National Institutes of Health, 1996 Data Fact Sheet: Congestive Heart Failure in the United States: A New Epidemic.

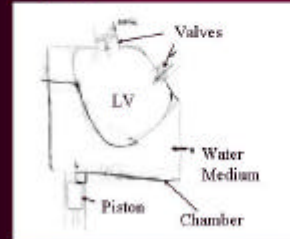
Application

- Our model will enable pre-clinical testing of catheters used to deliver gene therapy to the myocardium weakened by CHF
- Our project will allow modeling of flow through the aorta, contributing to a better understanding of in vivo fluid mechanics



Initial Design Concepts

- Pumping Mechanism



Pugh Chart

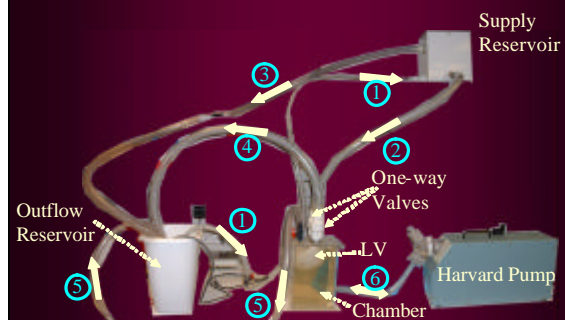
Design Requirements	Criteria Weighting	Design Concepts	
		Piston	Pneumatic Pump
Pulsatile flow	20	10	6
CHF LV geometry	20	10	10
Ability to directly visualize the catheter system	20	9	9
Heart valves (synthetic/tissue) that enable catheter access across it into LV	20	10	10
LV wall motion (5.8-7.0 cm short-axis/8.8-10.0 cm long-axis)	17	10	10
Adjustable heart rate (70-120 bpm)	17	10	6
Femoral access to the LV via the aorta	14	9	9

Blood analog perfused at body temperature (37°C)	12	10	7
Chamber capable of accommodating a worst case dilated CHF LV (9.0 cm short-axis, 12.4 cm long-axis)	12	9	9
Fluoroscope compatibility	12	9	8
Adjustable LV ejection fraction (15% -40%)	12	9	8
MR compatibility	8	8	8
Internal surface texture	8	8	8
Pressures comparable to internal human systolic/diastolic pressures (120/80 mmHg)	8	8	6
Weight		0.94	0.53

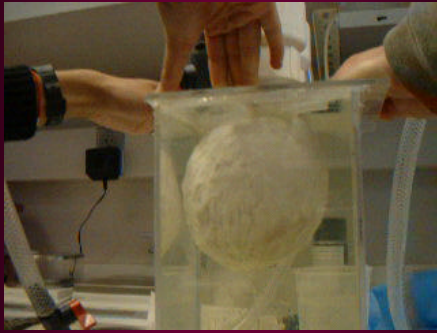
Initial Prototyping - Chamber & Flow System

- Purchase of all materials for initial prototype
- 3/16 inch Acrylic sheet cut using the PRL Lasercamm
- Tapped screw holes and placed adapter for valves and connections to tubing
- Written proposal to obtain tissue valves

Initial Prototyping - Chamber & Flow System

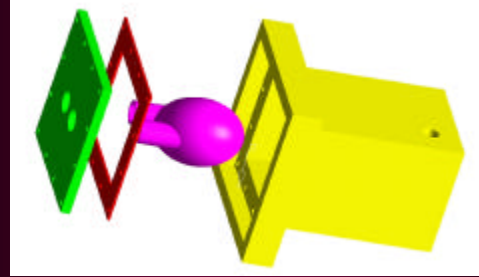


Initial Prototyping - Chamber & Flow System



Initial Prototyping - Chamber & Flow System

- Design for final chamber



Next Steps: Chamber & Flow System

- Finalize drawings of chamber and outsource design to a machine shop for manufacturing
- Work with current chamber prototype to improve flows and pressures of the flow system
- Integrate tissue valves into flow system
- Attachment of ventricle at chamber valve interface
- Testing and optimization of system

Initial Prototyping - Left Ventricle

- Latex Balloon



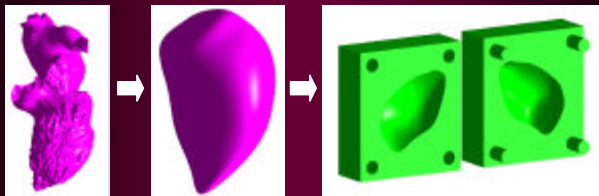
- Urethane Coated SLA



- Urethane and Sylgard samples for material testing

Initial Prototyping - Left Ventricle

- Modification of IGES file to create negatives of the model.
 - Reduction in size of model
 - Box created to surround the model and the model subtracted from the interior



Next Steps: Left Ventricle

- Perform Instron testing on materials to obtain stress-strain data
- Fit data to non-linear elastic model to obtain material parameters for Finite Element Analysis (FEA)
- FEA (Guidant) to determine best material for LV, i.e. material that will provide desired deformations and wall motion
- Final ventricle fabrication

Foreseen Challenges

- Attaching the tissue valves to the system
- Formation of final LV with varied wall thickness
- Competing wall thickness requirements
- Integrating the LV into the chamber
- Attachment of vascular model (provided by Guidant) to the final system

Final Deliverables

- Completed flow system that incorporates a deformable LV and Guidant's vascular model

- Timeline

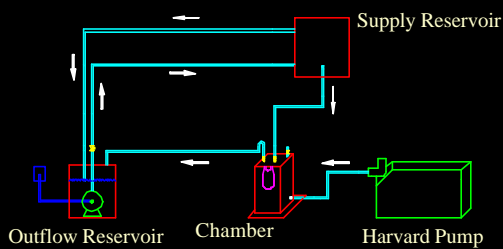
*April: Outsource Chamber Fabrication
Ventricle design (Material testing, FEA,
Valve incorporation, Prototyping)*

May: Design validation and optimization

June: Final Report and Presentation



Final Deliverables



Thank You
Any Questions?

7.2 Expenses

The following table shows our expenditures to date.

Table 5: Expenditures to date

Supplier	Items Purchased	Cost
McMaster Carr	Glue gun dispenser, O rings	\$44.00
Home Depot	Tubing, paint brushes, dust masks	\$11.75
Home Depot	Tubing, adapters, sealant	\$40.00
Gas Station	Gas	\$3.74
McMaster Carr	Hex nuts, check valve, adapter	\$39.33
Tap Plastics	3/16 in acrylic sheet, glue	\$26.09
Delphion	Patents	\$21.00
PRL (day pass)	day passes (3)	\$30.00
Kinko's	Binding of Report	\$20.00
	Total	\$215.91

The table below shows projected expenditures for next quarter.

Table 6: Projected Expenditures

Items to Be Purchased	Expected Cost
Outsourcing of Chamber to a Machine Shop	\$500.00
Materials for Final Chamber (tubing, screws, etc.)	\$100.00
Material for FDM of LV	\$300.00
Travel Expenses and Lunches	\$100.00
Instron Testing	\$200.00
Product Realization Lab Licenses	\$270.00
Fabrication of SLA Model	\$1000.00
Printing and Binding of Midterm and Final Report	\$50.00
Total	\$2520.00

7.3 Resources

A large number of human and physical resources have been utilized during the first stage of this design project, many of which will carry over into the next stage. Human resources include our team of advisors at Stanford and Guidant, who have helped the project team immensely with design specifics and also with the details of accessing physical resources on and off campus. Physical resources have also been vital for the initial prototyping and design development stages.

7.3.1 Human Resources

- ?? Stanford Mentor: Dr. Charles Taylor
- ?? Stanford Mentor: Mary Draney
- ?? FEA Experience: Dr. Chris Elkins
- ?? Guidant Team: David Wolf-Bloom, Jessica Chiu, and Deborah Kilpatrick
- ?? Company leaders: Dr. Scott Delp, Dr. Tom Andriacchi, Nikhil Batra

7.3.2 Physical Resources

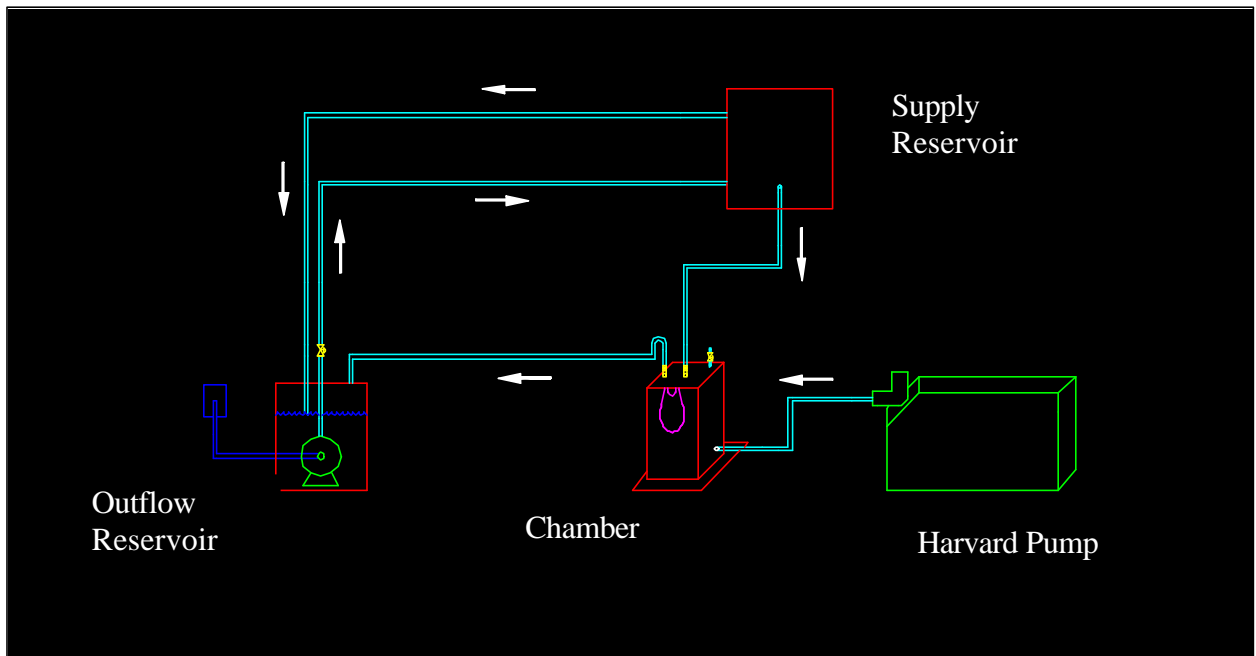
- ?? Equipment and software programs: Dr. Taylor's Laboratory
- ?? LV and artery materials: Guidant Preclinical R&D Dept
- ?? Fabrication processes: Guidant Preclinical R&D Dept
- ?? CHF LV image data: Guidant New Ventures Dept (2D Echo), Stanford (MRI/CT)
- ?? Computer Software: Stanford University
- ?? Machine Shop Tools: Stanford University
- ?? Instron with heating chamber: VA Hospital or at Guidant

7.4 Patent Search Information

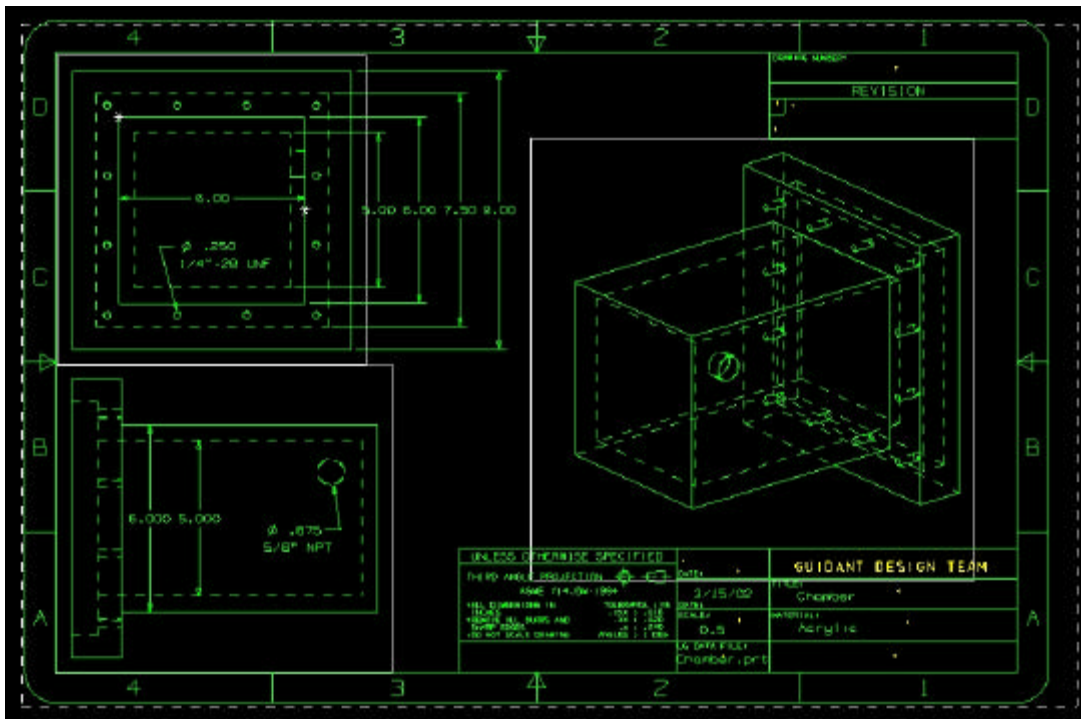
Table 7: Relevant Patents

US Patent No.	Date Issued	Title	Description	Contact Info
US4639223	1/27/1987	Simulated heart display system	A system for simulating the activity of the heart that includes a computer controlled heart model for generating and displaying simulated electrogram signals.	Keller, Jr.; J. Walter, Miami, FL 3143
US5692907	12/2/1997	Interactive cardiac rhythm simulator	A heart display system, where a computer is operable to simulate different selected hearts, each with a different pattern of electrophysiological pathways,	Glassel; Philip R., Stacy, MN; Miller; Michael D., Minneapolis, MN
US6058958	5/9/2000	Pulsatile flow system and method	Pulsatile flow system that includes a reservoir, a pressure riser and a first fluid passage connected between the reservoir and the pressure riser.	Benkowski; Robert J., Houston, TX; Lynch; Bryan E., Houston, TX
US3639084	2/1/1972	Mechanism for Controlling Pulsatile Fluid Flow	An apparatus for imparting a pulsatile flow to fluid in a conduit, which has pumping means for providing the pulsatile flow of fluid therein.	Goldhaber; Richard Paul, Chicago, IL
US4976593	12/11/1990	Pulsatile flow delivery apparatus	A pulsatile flow delivery apparatus that includes a horse shoe shaped raceway, a tube, a milking mechanism, an occlusive clamp and a control device.	Miyamoto; Alfonso T., Fukuoka, Japan
US4450710	5/29/1984	Device for testing heart valve prostheses	A device for hydrodynamic, in vitro testing of heart valve prostheses.	Nettekoven; William S., White Bear Lake, MN
US5924448	7/20/1999	Infinitely variable pneumatic pulsatile pump	A pulsatile pump for which the output is infinitely variable between a slow pulsatile flow and a sharply pulsed flow rate.	West; Joe E, Maridian, TX
US5306295	4/26/1994	Electrohydraulic heart with septum mounted pump	A total artificial heart for placement inside a living body comprising right and left ventricle enclosures, wherein each ventricle includes an exterior wall formed of (i) contacting wall structure and (ii) non-contacting wall structure which collectively enclose an interior volume comprised of a blood chamber and a pumping chamber. chamber and thereby simulate natural pumping action of the heart.	Kolff; Willem J., Salt Lake City, UT; Topaz; Stephen R., Salt Lake City, UT; Topaz; Peter A., West Lafayette, IN; Bishop; N. Dan, Salt Lake City, UT...

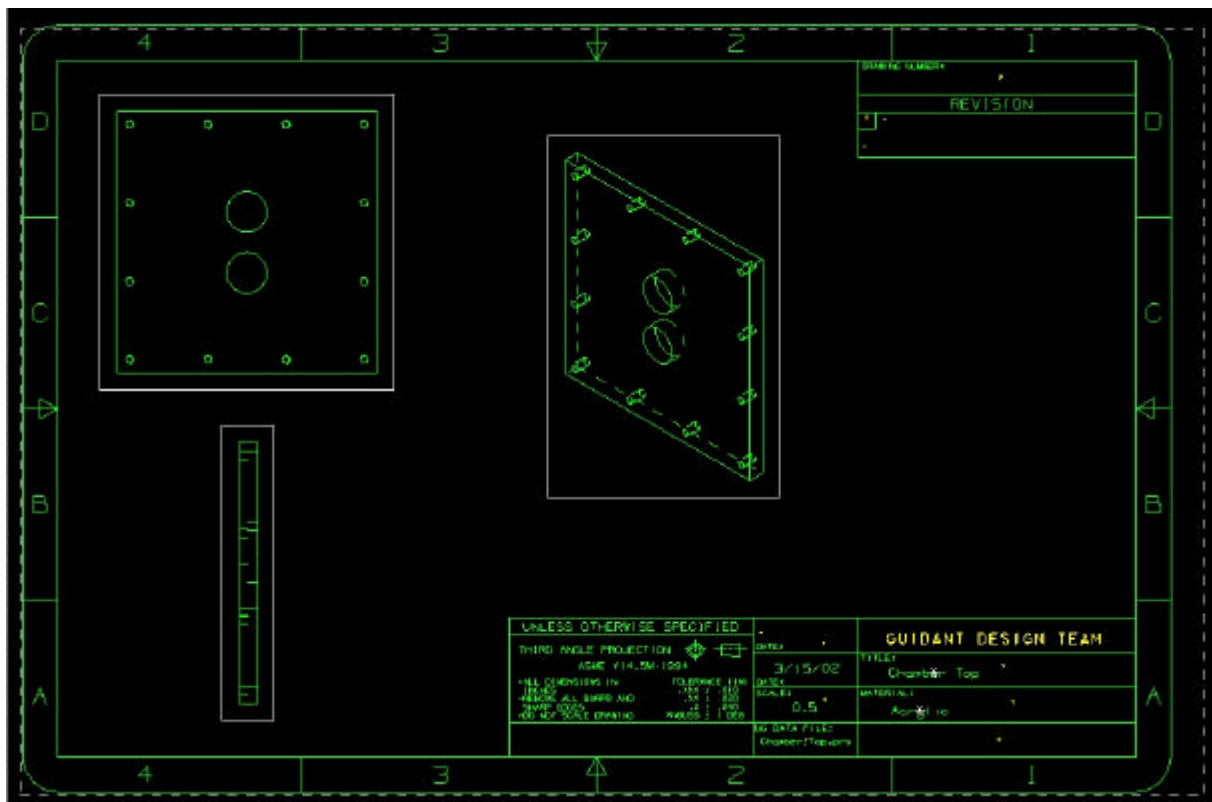
7.5 Design Sketches



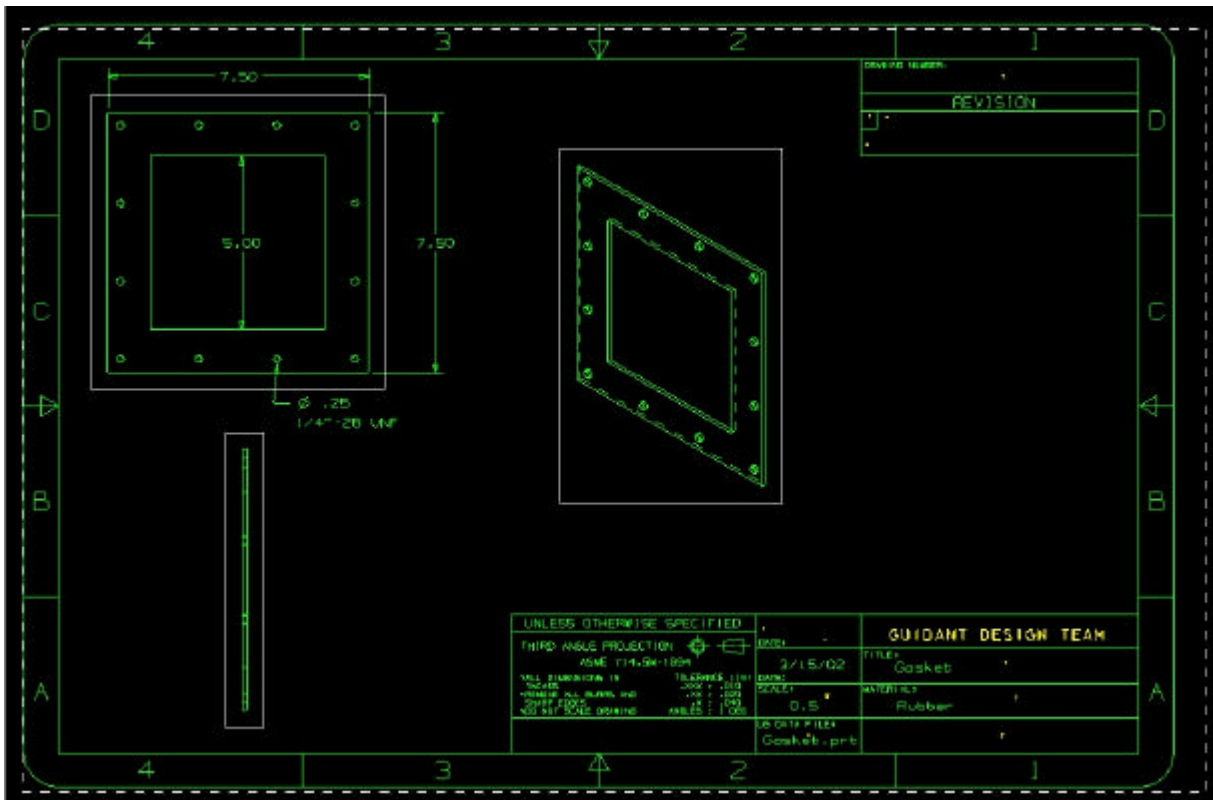
Schematic of Flow System Used in CHF Model



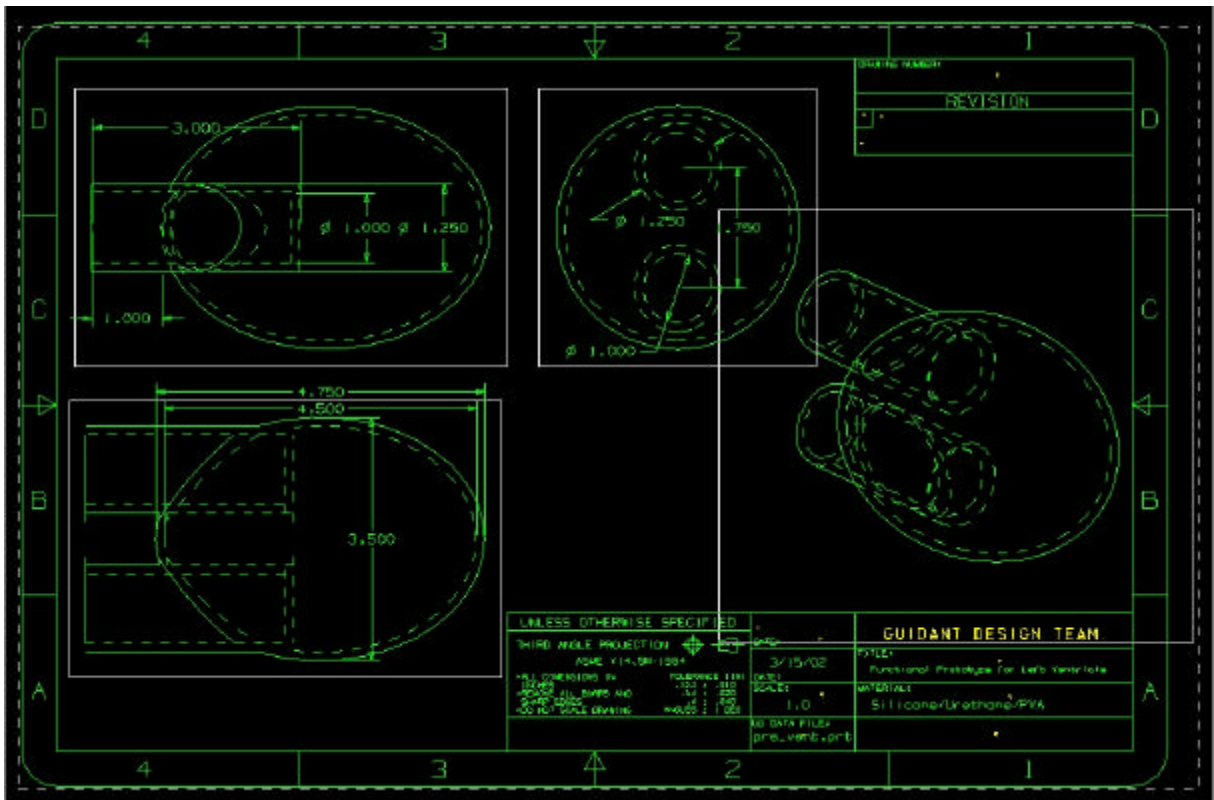
Unigraphics Generated Design of Chamber Base



Unigraphics Generated Design of Chamber Top



Unigraphics Generated Design of Gasket Seal



Unigraphics Generated Design of Ventricle Prototype

7.6 Original Sponsor Descriptions

7.6.1 Design Description

The cardiac anatomy of congestive heart failure (CHF) patients can be extremely altered from the normal configuration, leading to major changes in ejection fraction, synchronicity, and overall cardiac biomechanics. This presents a significant challenge in the early R&D phases of device-based therapies for CHF, since the preclinical test methods and models typically used for intraventricular access no longer fully apply. This project will seek to develop a new, dynamic heart model that could be used for early prototype testing of intraventricular device access in the CHF left ventricle (LV). The students will use medical imaging data from both echocardiography and MRI of CHF patient hearts over the cardiac cycle to define design parameters for the in vitro heart model. Ultimately, a system will be developed for dynamic testing of Guidant's existing prototypes for intraventricular access devices. This project will expose students to the complex disease of CHF and the use of state-of-the-art imaging analysis techniques to study the biomechanics of the failing heart. The project will challenge students to develop a dynamic simulator of a CHF heart model for catheter system performance evaluation.

7.6.2 Goals of Project – Final Deliverables

To develop a clinically-realistic simulated dynamic left ventricle (LV) heart model with the following features:

- ?? CHF LV geometry
- ?? LV wall motion
- ?? Femoral access geometry to the LV via the Aorta
- ?? Blood analog perfused at body temperature
- ?? Ability to directly visualize the catheter system for observation-allow the catheter-wall contact location to be recorded by video and the contact pressure measured (a “nice to have”).
- ?? Adjustable heart rate: 70-120 bpm
- ?? Adjustable LV ejection fraction: 0.15 – 0.55 (via LV and HR drive mechanism/control system)
- ?? Heart valves (synthetic or tissue), valve enables device access across it into LV
- ?? Expansion chamber capable of accommodating a worst case (dilated) CHF LV

Final deliverables include a working prototype of CHF LV simulation model, design documents/specifications and future recommendations

7.7 Checklists from Executive Committees

Regulatory and Standards Checklist

1. What is your project?

Please briefly describe the project you are working on:

Guidant: Design of a Clinically Realistic CHF Left Ventricle Model

Please describe potential solutions that you are considering for your project:

Single Piston, Pneumatic Pump, Multi-Piston, Collapsible Ring, and Multiple Bladder Mechanism (see report for details)

List and briefly describe any potential solutions that have biological or chemical components.

None

List and briefly describe any solutions that emit radiation.

None

2. Project Scope

List which solutions involve developing a completely new device.

None

List solutions reusing a known technology, approach, or process.

Single Piston, Pneumatic Pump, Multi-Piston, Collapsible Ring, and Multiple Bladder Mechanism

Are any solutions based on other devices?

Yes

If so which devices?

Pneumatic pumps, pressure chambers, vacuum chambers, custom bladders, static models of the heart, pulsatile flow mechanisms

Were the device(s) developed before 1976?

Yes

How are they similar?

Uses same mechanisms, except tries to incorporate multiple devices into one dynamic model

Does your solution pose any new risks?

No

Utilize any new technologies?

Detailed wax molds of left ventricle created from cadaver CHF hearts, left ventricle model that replicates *in vivo* wall motion

Are any of your solutions used with other devices or treatments?

Yes.

If so, what devices or treatments?

The final model will be used to test the maneuverability of Guidant's catheter based systems.

Are they life critical?

The purpose and setting of the model will be more for diagnostic and research use.

3. Safety

Does your project pose any dangers to patients, physicians, or others?

Not unless the purpose of the devices is ultimately used to validate and design future catheter systems.

If so, how?

If the model precludes need for studies (i.e. animal trials) previously conducted on catheter systems to obtain FDA approval, it will have to maintain the high standards required for testing.

Is it life threatening?

No

4. Sponsor recommendations

What classification does your sponsor want your group to aim for?

Not subject to FDA approval. If the device is not used for validation and design purposes, model must be show to be represent *in vivo* conditions.

What premarket approval process do they envision for your project?

None

5. Assuming your project is a device:

This last section of the checklist is intended to help start your project's FDA identification/ classification process and to document your progress. In order to guide you through this process, this document utilizes the FDA website's device advisor (see

step 1). Note: at various points along the process the website offers more information to help you answer questions; these questions/links are not in this checklist.

Steps:

- 1) Open <http://www.fda.gov/cdrh/devadvice/31.html>
- 2) Does the product emit radiation? **No**
- 3) Does Your Product Meet the Definition of a Medical Device? **No**
- 4) Do you know the class of your device?
 - a. If yes jump to 5
 - b. If no:
 - i. Read section on “How to determine Classification”
 - ii. Use the Classification Database or the Device Panels (circle which you used)

- 5) Record the following information:

Device: **Clinically Realistic CHF Left Ventricle Model**

Medical Specialty: **Cardiovascular**

Product Code: **no product on the market**

Device Class: **N/A**

510(k) exempt?: **No**

Regulation Number (7 digit): **no product on the market**

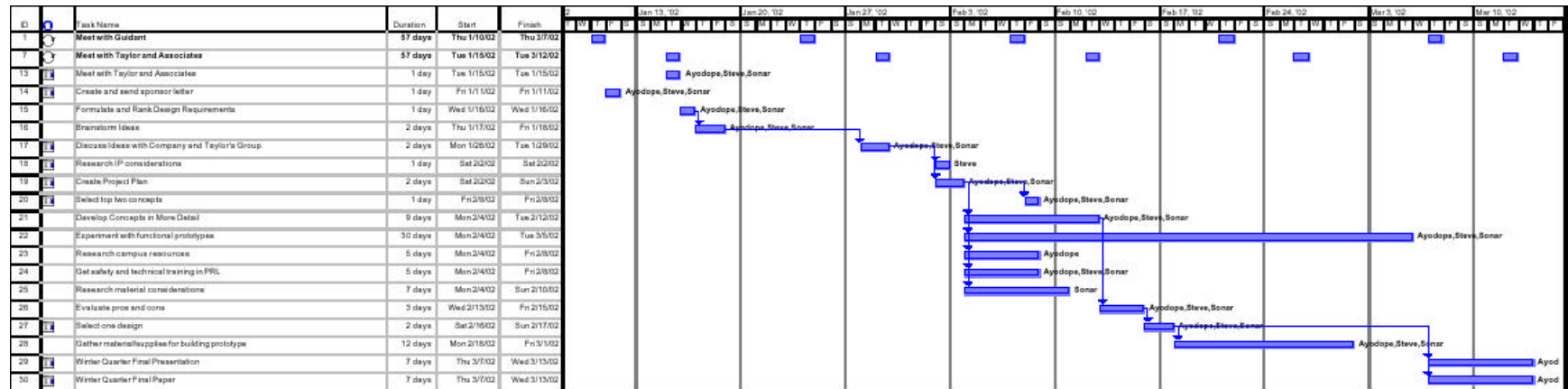
Device Description: **no product on the market**

- 6) Which are required: 510k / PMA / **Exempt**
(circle which apply – known from the above classification)

The next steps in the regulatory process depend greatly on your specific project. See the regulatory team for guidance if you are uncertain of your next steps.

7.8 Gantt Chart for Winter and Spring Terms

Winter Term



Spring Term

