EML 4551 Design Organization

A B.S. THESIS
PREPARED IN PARTIAL FULFILLMENT OF THE
REQUIREMENT FOR THE DEGREE OF
BACHELOR OF SCIENCE
IN
MECHANICAL ENGINEERING

Experimental Verification of Optimized Cooling of Human Hearts for Transplant Surgery

25% Report

Patricia Matthews
Rebekah Santana
Rafael Sanz
Marcelo Torrentes

Advisor: Professor George Dulikravich

April 12, 2013

This B.S. thesis is written in partial fulfillment of the requirements in EML 4905.
The contents represent the opinion of the authors and not the Department of
Mechanical and Materials Engineering.

Ethics Statement and Signatures

The work submitted in this B.S. thesis is solely prepared by a team consisting of Patricia Matthews, Rebekah Santana, Rafael Sanz, and Marcelo Torrentes and it is original. Excerpts from others' work have been clearly identified, their work acknowledged within the text and listed in the list of references. All of the engineering drawings, computer programs, formulations, design work, prototype development and testing reported in this document are also original and prepared by the same team of students.

Patricia Matthews Team Member	Rebekah Santana Team Member	Rafael Sanz Team Member	Marcelo Torrentes Team Member

Dr. George Dulikravich
Faculty Advisor

Table of Contents

List of Figures

List of Tables

Abstract

The primary objective of this project is to design a synthetic human heart for testing with the eventual intent of increasing the expediency of human hearts suitable for transplantation. The artificial heart will be made to have geometry and thermal properties as similar as possible to a real-life human heart, therefore the material selection process will be an essential aspect of this project. Analytical data and results will be collected from tests performed on the manufactured model. Additionally, a container will be constructed to preserve the human heart and perform simultaneous internal and external cooling of the human heart to yield as uniform a temperature distribution through the organ as possible. Necessary pumps and thermistors will be selected to measure cooling trends throughout the model.

Introduction

Problem Statement

With current technology, human hearts fit for transplant are only viable for approximately four hours. However, an improved cooling method would increase the lifespan of the heart, which would give medical personnel a better opportunity to transport the heart in time to save a life. Research shows that there is an optimal cooling rate for each type of tissue that maximizes cell survival, but external cooling alone is not sufficient to achieve it. With external cooling alone, inner tissues are not cooled as quickly as outer tissue. This gradient causes thermal stresses and increases the rate of decay. Therefore, we propose a system to cool the heart both externally and internally by pumping fluid in and around the heart order to reduce thermal stresses, which should prevent decay and in turn, increase the lifespan of the heart.

Project Objectives

- Construct an approximate geometric model of the human heart from a material which emulates its physical properties accurately.
- Develop a double-chambered container within the heart that models the internal fluid flow, and feed cooling liquid into it at a controlled flow rate and temperature in order to test the effectiveness of internal cooling.
- Design a responsive, controlled system using a mechatronic flow rate controller connected a computer and to thermistors and cooling valves within the model.
- Construct a shatterproof, transparent and safe box for heart transport.

Motivation

The process of organ preservation has long been a key issue for doctors and surgeons attempting to provide suitable organs to patients in need. Current methods are limited to short shelf lives and run the risk of tissue degradation due to oxygen deprivation. The falling number of viable donors suggests that more sustainable techniques are needed to offset demands. By producing an apparatus that can efficiently cool the heart uniformly, it may be possible to double the amount of time the heart is useable and transported to recipients, as well as ultimately increase the availability of organs fit for transplantation.

Literature Survey

Background

The first human-to-human cardiac transplantation was performed in South Africa on December 3, 1967 by surgeon Christian Barnard using the experimental work developed by Norman E. Shumway. This event marked the beginning of heart transplantations worldwide and the development of several methods and techniques of preserving organs outside of the body. These techniques fall into two major categories: keeping the heart in human physiological state and freezing the heart until transplant (Brink & Hassoulas, 2009).

Relevant Research

The most widely used method for transporting organs is a standard ice cooler. Cold static preservation is still the most prominently used method for organ transportation because it is simple and easily reproduced. The organ is submerged in a sterile liquid solution and surrounded by ice packs at about 4 degrees Celsius. This method, however, has its drawbacks; studies have shown that external cooling of organs is a vastly ineffective method of organ preservation due to the lack of uniform cooling that occurs when using ice packs. Additionally, ice packs alone may be insufficient in cooling an organ down to a target temperature rapidly enough (Dennis, Eberhart, Dulikravich & Radons, 2003).

More technological developments have been made in recent years. In 2010, a research team at the University of California Berkley’s Ronald Reagan Medical Center developed a device capable of preserving a human heart in near perfect physiological state. The medical device developed by TransMedics restores the donor’s heart back into a beating state by pumping oxygenated blood through the system at stable temperatures all while monitoring the heart’s functionality (Albin, 2010). As recently as March 2013, the first ever “warmed liver” transplant was performed in London, England by a surgical team at King’s College Hospital. The new innovation is the result of 20 years of research and work done by engineers at Oxford University. The device used to preserve the liver pumps blood through the capillaries of the liver, causing the organ to regain color and normal functionality (Walsh, 2013). These technologies are still in early developmental stages.

The process of cryogenics is delicate, as high cooling rates in donor organs can cause strong residual thermal stresses which may severely damage organ tissue, and low cooling rates may lead to chemical decomposition of the organ. Research shows that for structures of impure chemical composition, such as muscle tissue, the physical phase changing process occurs over a wide range of temperatures as opposed to any single temperature (Dennis & Dulikravich, 2000). Studies have been conducted to determine the optimal local freezing rate of an organ, that is, the quickest freezing rate that can be obtained while keeping the amount of local thermal stresses endured by the specimen below the limit where fracture occurs.

Sophisticated computer simulation programs have been developed to accurately determine the variation of unsteady three-dimensional temperature distributions on the walls of the organ. Tests were done using various materials with similar size and shape of a kidney. The tests showed that damages due to thermoelastic stresses could be controlled and minimized by optimizing the temperature distribution on the surfaces of the freezing container used in preserving the organ (Dennis & Dulikravich, 2000) (Dennis, Dulikravich & Rabin, 2000).

Properties

To ensure accuracy, the physical model of the heart should be made from a polymer that emulates actual heart tissue. Researchers at Imperial College London have synthesized a material called poly(glycerol sebacate) (PGS) which, at a range of temperatures, yields mechanical properties similar to that of myocardium, the muscle substance of the heart. Their findings are summarized and compared to data for human heart tissue, which will heretofore be referred to by its proper medical name, myocardium, below:

Properties	**PGS**	**Myocardium**
Density	1.1277 to 1.1394 g/cm^3	approx. 1.055 g/cm^3
Young’s Modulus	0.04 to 1.2 MPa	10 to 500 kPa
Tensile Strength	0.2 to 0.5 MPa	--

Table 1: Properties

Since the Young’s modulus for PGS is similar to that of a real heart throughout diastole, PGS is a promising material substitute for myocardium (Chen, Bismarck, Hansen, Junaid, Tran, Harding, Ali & Boccaccini, 2008) (Vinnakota & Bassingthwaighte, 2003).

Design Alternatives

Overview

Modeling the human heart presents unique challenges in terms of both geometry and physical properties. With regard to shape, the heart is not particularly symmetric in any dimension. Furthermore, the thickness of the myocardium tissue varies significantly across the heart. The structure will also vary with respect to time, as the heart beats. The heart beats several times a minute and the rate depends on the requirements imposed by the body. While the heart will not be beating as it is being delivered to a transplant, the heart is capable by nature of expansions and contractions. An average wall thickness will need to be calculated that will accurately reflect the environment that the heart will experience while it is being transferred from donor to recipient. The veins and arteries connected to the heart also present a similar challenge. Veins and arteries do not have a fixed diameter since they expand and contract as blood pumps through them. These will also need to be averaged. Furthermore, the chambers within the heart also vary in volume and there are various valves between chambers that affect blood flow. The four chambers within the heart will be reduced to two and the valves between them will be ignored. With regard to their physical properties, they will also need to be averaged, as the tissue and cross-section is not constant throughout. While thermal properties of the human heart exist and can be found, they are not found easily. Several hours have been spent and most of the literature available utilizes data on canine and pig hearts since those are more readily available for testing. Human data will be used where possible and animal data where needed.

Design Alternative 1

For the first design consideration, several geometric configurations were significantly simplified in order to better assess the most important heart characteristics and allow for the simplest manufacturing. A two chambered box layout was considered with simplified inlets and outlets for coolant flow. The advantages for such a design are as follows: simplified modeling with quicker simulation time, ease of manufacturing, and ease of testing. While qualitative information could be drawn from the simplified model, it is a concern that such a model may not sufficiently simulate the behavior of the heart. The disadvantages are: a square geometry does not approximate the roughly conical shape of the heart accurately, the constant thickness of the chambers is not consistent with the varying thickness present in real hearts, and the inlets and outlets are all the same diameter which will affect the flow through the heart and the resultant cooling characteristics.

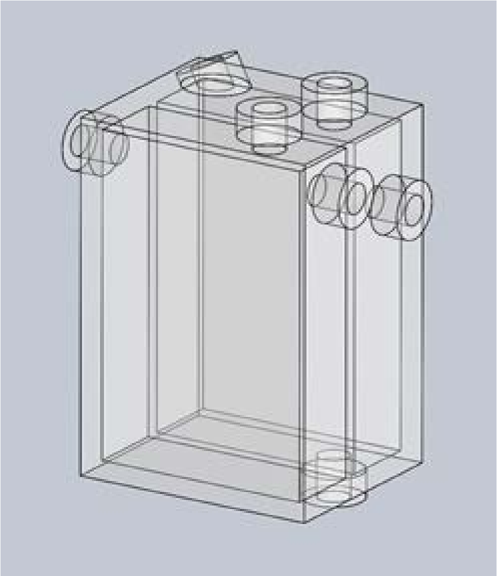


Figure 1: Design Alternative 1

Design Alternative 2

For the next design consideration, several of the edges were rounded and the shape of the two chambers was altered to be more elliptic and not as square. The thickness is not constant throughout the model and the placement of the inlets and outlets was changed slightly. The more rounded shape and inlets and outlets more closely resemble the human heart than the first design alternative while still allowing greater ease of manufacturing than a more exact replica of the human heart would allow. Even so, manufacturing this second alternative will be more involved than the first. The advantages are: simplified modeling with quicker simulation time, ease of manufacturing, ease of testing, and more accurate results than the first alternative. The disadvantages are: slightly longer modeling, more difficult manufacturing, more involved testing and still quite different than the actual human heart.

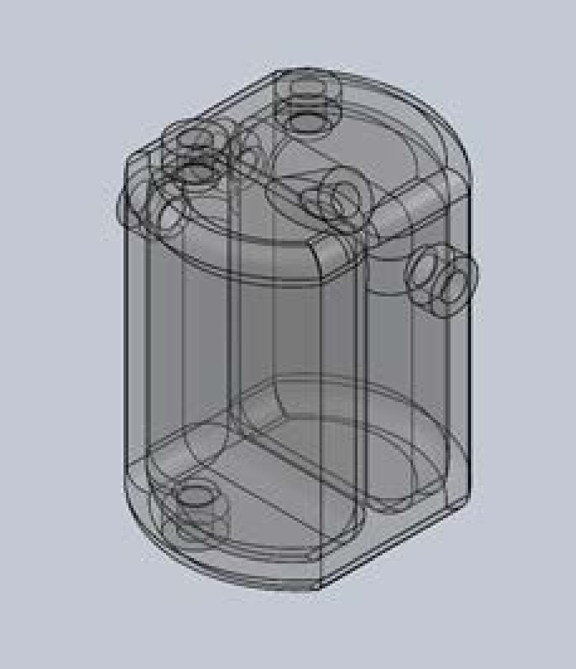


Figure 2: Design Alternative 2

Design Alternative 3

The last design consideration involves modeling the heart as closely as possible while still being feasible to model, simulate, manufacture, and test. The entire shape of the heart is symmetric across the vertical axis which, while not true for a true human heart, is suitable for our purposes. The advantages of the design are: more closely resembles heart than previous two, still easier to model, test, and manufacture than a real heart, and the inlets and outlets are placed in much more accurate positions. The disadvantages are: significantly longer modeling time, much more complicated manufacturing, and more difficult to test. The largest challenge to this design is the feasibility of producing and testing it.

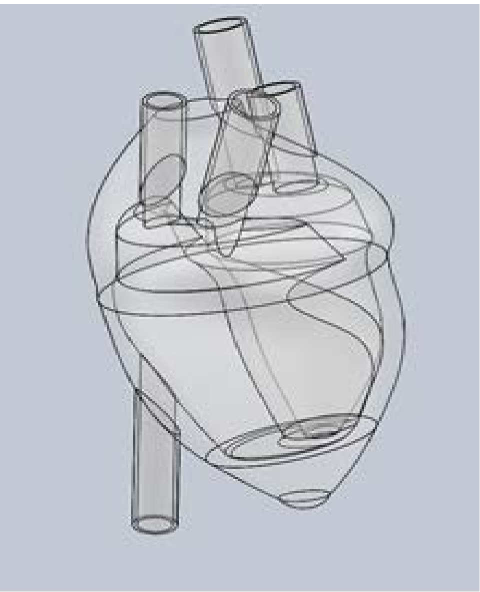


Figure 3: Design Alternative 3

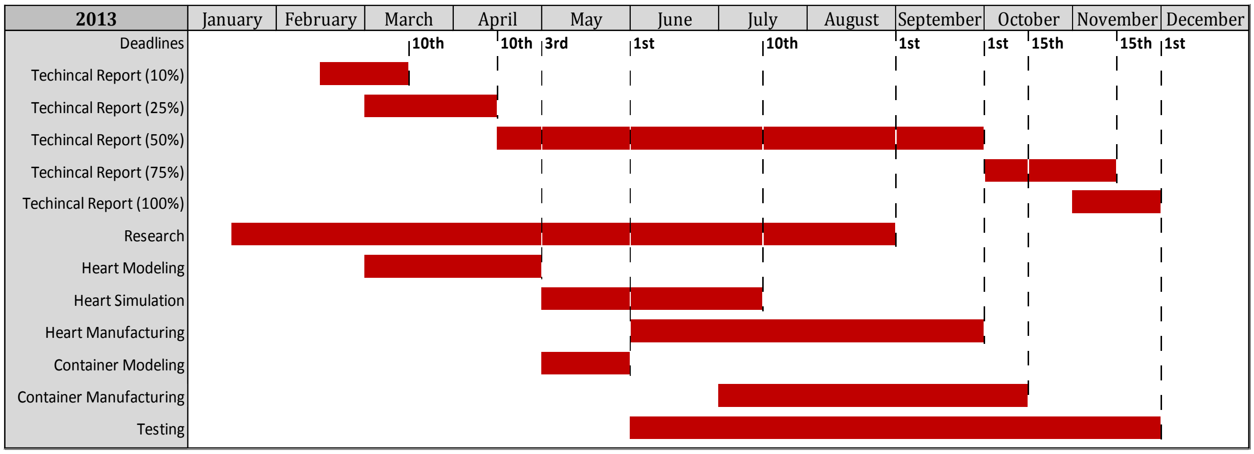
Proposed Design

Initially, Design Alternative 3 was chosen because despite the difficulty in producing it, it most accurately reflects the characteristics of the human heart and accuracy is paramount to this project. However, we were donated an even more realistic CAD model of the human heart and will be basing our physical model off of its design. While the design may need to be slightly altered during manufacturing, it should not pose any insurmountable difficulties in manufacturing and testing. The model will be made of a see-through material that closely resembles the mechanical properties of an actual human heart. A test chamber will be developed and we may implement cooling fluids that change color with temperature to see the heat distribution within the heart. The temperature at various points throughout the heart model will be measured over a set period of time.

Project Management

Timeline

Table 2: Project Timeline



Breakdown of Responsibilities

To date, each member of the team has logged approximately twenty hours of work on this project, and we are projected to each spend roughly sixty more before the work concludes.

Table 3: Breakdown of Responsibilities

	Rebekah Santana	Patricia Matthews	Marcelo Torrentes	Rafael Sanz
Modeling	🟥			🟥
Research		🟥	🟥	
Fabrication	🟥		🟥	
Design				🟥
Material Selection		🟥		
Simulation				🟥
Fundraising	🟥			
Record Keeping		🟥		
Testing Apparatus			🟥	

Analytical Analysis

Testing

The temperature profile throughout the heart is of the upmost importance. If any tissue cools below its freezing temperature it becomes permanently damaged and the heart is rendered useless. On the other hand, if the tissue is too warm, then decay begins to take place which may also cause irreparable damage to the heart. A uniform cooling of the heart, which will be characterized by uniform temperatures, is the very purpose of this project. Thermisters, thermometers, and various other temperature reading devices, will be utilized to obtain measurements throughout the heart.

Criteria

Convergence

We intend to test multiple models of the same heart to demonstrate that the same trends are developed, showing consistency and reliability of the results. Ideally, other researchers would be able to come up with similar results when repeating the tests or running simulations.

Tolerance

While it is understood that there may be discrepancies between physical models, if they are too large then certain specifications were not met. The results need to be appropriately similar. If they are not, then one or both models are defective. While matching two models poses challenges, it allows for comparison. Sources of error could include slight differences in manufacturing conditions, especially if the molding process involves the use of two separate parts to make the whole heart model.

Accuracy of Trends as Opposed to Accuracy of Values

While close values in both models is valuable, the most importance is convergence of the results. There is a larger window for error in exact results as opposed to the behavior of the results.

Major Components

The selection of the material and method of fabrication of the synthetic heart will be a main component of this project. Several polymers and plastics must be considered and evaluated to match the properties of the human heart. Lost wax casting, reverse silicon molding, and cavity printing will be considering in manufacturing the artificial heart tested.

The perfusion apparatus will contain a pump, piping system, transparent walls, and insulation. The pump will be selected to have a low flow rate and variable speed. Thermistors will also be used during testing in order to monitor temperature at key points throughout the model. The coolant we will use will be either water, ice water, or a saline solution.

Cost Analysis

Sources of Cost

For this project there are four key sources of cost and income: Design Cost, Prototype Cost, Travel Costs, and Fundraising. These costs will be considered in terms of time and monetary costs. An appropriate budget and careful specifications of costs allow for a better planned project. It is essential to plan all costs, both monetary and time, carefully.

Design Cost

Design costs usually consist of overhead costs and salaries. Since this team is composed of students, the costs can be considered time costs exclusively in terms of how many man hours each team member must put in. The man hours will be listed in terms of research, modeling, testing, report writing, and presentation preparation and delivery.

Prototype Cost Analysis

The physical model of the heart can be produced in several ways. One possibility is the lost-wax method. By this method, the CAD model would be 3-D printed in wax. The piece would then be placed into a container and packed tightly with sand, and heated. This would cause the wax to melt and drain out, leaving a cavity which could function as a fill mold for the selected modeling material. The main problem with this approach is that it is best suited for solid models, not the mostly hollow structure we would need it to produce.

Another option would be to 3-D print the model in plastic resin and cut the result in half. Each half could be covered in silicon, which would solidify into a flexible reverse mold. The concern with this method would be that the piece would have to be reassembled. The last option considered would be to re-model the heart as a negative and 3-D print the cavity, which would then be filled with the material.

Either of these methods should cost about the same, but realistically they do not. The second option would be by far the least expensive, as it can be achieved in-house. The printing process for our prototype would necessitate eleven cubic meters of resin, which will cost around $180. In addition to the materials, the print would take almost twenty hours. Altogether, produced at the Florida International University machine shop, the resin print of the model would cost around $250. Including overhead, the cost of printing at an outside firm would be close to three times as much as this. Even though wax might be less expensive, the benefit would be negligible.

As the material from which to construct the model has yet to be determined, any further estimations as to the cost would be arbitrary at this early stage.

Travel Costs

Travel to and from school to work as a team will be a source of cost, as each member lives an average of forty minutes away. Furthermore, sponsors will be sought out and will have to be visited. It must be expected that some may live a significant distance away from the Miami area.

Funding

Funding is a major aspect of any project, especially an engineering project involving organ simulation that must be as accurate as possible. When possible, potential sponsors will be asked for aid in order to help fund this project. Potential sponsors include nearby hospitals, clinics and professors from the biomedical department. Also, team members will regularly apply for online scholarships and awards and contribute the proceeds to the project. Finally, any remaining funding will be covered by the team members themselves.

Projected Costs

Category	Task	Time (hours)	Category Total
Research and Design	General Heart Research	80	440
	Heart Mechanical Properties Research	40	
	Heart Thermal Properties Research	40	
	Artificial Heart Manufacturing Research	30	
	Material Research	50	
	Research of Testing Methods	40	
	Conceptual Designs	30	
	Solidworks Modeling	30	
	Comparison of Designs	10	
	Heart Container Research	30	
	Heart Container Design	20	
	Heart Design Optimization	20	
	Container Design Optimization	20	
Analysis, Assembly, & Testing	Computer Simulations	25	175
	Assembly of Heart and Container	30	
	Test Probe Placement and Testing	20	
	Physical Testing	40	
	Analysis of Data	40	
	Testing Optimization	20	
Reports & Presentations	Senior Reports	80	150
	Presentations & Rehearsals	30	
	Engineering Drawings	20	
	Posters	20	
		Total Hours	**765**

Table 3: Projected Time Cost

Project Section	Item	Cost
Materials & Components	Heart Material (Polymer/Gellatin/Plastic)	$100.00
	3-D Printing	$300.00
	Thermistors	$20.00
	Clamps	$10.00
	Tubing	$20.00
	Electrical Wiring	$20.00
	Coolant (Water or Saline Solution)	$5.00
	Polycarbonate Sheets	$20.00
	Pump	$100.00
	Power Supply (salvaged)	$0.00
Report & Presentation	Poster	$80.00
	Reports	$20.00
	Miscellaneous (props, supplys, etc)	$10.00
	Projected Total Cost	$705.00

Table 4: Projected Monetary Cost

Prototype System Description

Synthetic Heart

The primary objective of this project is to create a synthetic heart that can accurately simulate the physical behaviors of a human heart. It is necessary for the synthetic heart to resemble the 3-dimensional CAD drawing provided in order to have more realistic results. The synthetic heart must be constructed with thermal properties similar to that of actual heart tissue. This is essential in order to accurately simulate and test the system under realistic parameters. One of the challenges in finding a suitable polymer solution that will yield muscle-like properties is to have the final product contract and expand in the same manner as a real heart would. Research shows that a protein found in insects known as resilin is capable of having similar elasticity of human muscle tissue (Cebe, Hu, Kaplan, and Qin). Obtaining this substance for fabrication of the synthetic heart would be desirable.

The artificial heart must also have the size and geometry of a real heart, including two internal chambers that will act as the right and left ventricles and walls with approximately the thickness of myocardium. These components factor into the heat conduction and cooling of the model especially since perfusion will be conducted to transport the coolant throughout the entire heart. The heart model should have a mass of approximately 250 to 350 grams and roughly the size of an adult male’s closed fist. The structure produced will also endure a wide range of temperature change. Initially, the synthetic heart will be kept near physiological conditions, or about 37°C. The heart will be then taken, placed into the cooling container and cooled down to very low temperature that will be determined through computerized simulations. After the synthetic heart reaches near freezing temperature, the heart will be kept at a stable condition. As a final step, the heart will be gradually warmed back to normal body temperatures and removed from the apparatus.

Perfusion Apparatus

The heart preservation container will serve as the both a hypothermic perfusion apparatus and monitoring device. The appropriate pump and tubing system must be selected to achieve appropriate flow rates of the fluid through the vessels while maintaining the desired cooling temperatures. The pump should be able to provide a flow rate that does not exceed roughly 5 liters per minute, which is the approximate flow rate of blood through an adult human heart. The pump and tubing will be sized to fit the model appropriately. The container will have several electrical components aimed at ensuring the safety of the heart during the cryogenic process and transportation. To accomplish this task, a digital interface will be used to display the temperature inside the container at all times. Multiple thermal probes will be strategically placed on the synthetic heart to measure the behavior of the polymer as the temperature drops to near freezing levels. Organs under low temperature conditions can suffer large amounts of thermal stresses and stain that can damage the muscle tissue and render it useless and unfit for transplantation. Subsequently, stress and strain sensors must be placed on the tested samples to confirm that the loads applied on the heart does not surpass its threshold.

Plans for Testing Prototype

The physical models will be tested to demonstrate that it is possible to cool a human transplant heart in a manner that reduces thermal stresses within the heart and prevents tissue decay.

Multiple models of the heart will be cooled using a given flow rate and fluid temperature, measured at pre-determined points within the heart via thermistors. Results will be analyzed to show differences between external cooling and combined external and internal cooling.

References

Albin, A. (2010, December 06). 'beating heart' technology could revolutionize field of heart transplantation.*UCLA Newsroom*. Retrieved from http://newsroom.ucla.edu/portal/ucla/ucla-led-study-of-beating-heart-165987.aspx

Brink, J. G., Hassoulas, J., Chris Barnard Division of Cardiothoracic Surgery, J., University of Cape Town, , & Groote Schuur and Associated Academic Hospitals, (2009). The first human heart transplant and further advances in cardiac transplantation at groote schuur hospital and the university of cape town- with reference to : the operation. a human cardiac transplant. *Cardiovascular Journal of Africa* , *20*(1), 31-35.

Chen, Q., Bismarck, A., Hansen, U., Junaid, S., Tran, M. Q., Harding, S. E., Ali, N. N., & Boccaccini, A. R. (2008). Characterisation of a soft elastomer poly(glycerol sebacate) designed to match the mechanical properties of myocardial tissue.*Biomaterials*, *29*, 47-57.

Cebe, P., X. Hu, D.L. Kaplan, and G. Qin. "Mechanism of resilin elasticity." *Nat Commun*. 3.1003 (2012): Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22893127>.

Dennis, B. H., & Dulikravich, G. S. (2000, March).*Determination of unsteady container temperatures during freezing of three-dimensional organs with constrained thermal stresses*. International symposium on inverse problems in engineering mechanics.

Dennis, B. H., Dulikravich, G. S., & Rabin, Y. (2000).*Optimization of organ freezing protocols with specified allowable thermal stress levels*. In Scott, E.P. and Bischof J.C. (Eds.), *Symposium on Advances in Heat and Mass Transfer in Biotechnology* (pp. 33-48).

Dennis, B. H., Eberhart, R. C., Dulikravich, G. S., & Radons, S. W. (2003). Finite-element simulation of cooling of realistic 3-d human head and neck.*Journal of Biomechanical Engineering*, *125*.

Vinnakota, K. C., & Bassingthwaighte, J. B. (2003). Myocardial density and composition: A basis for calculating intracellular metabolite concentrations.*Am J Physiol Heart Circ Physiol*, *286*,

Walsh, F. (2013, March 15). 'warmed liver' transplant first.*BBC News*. Retrieved from http://www.bbc.co.uk/news/health-21788533