Submission 1

Engineering World Health 2014 Design Competition

Team Members:

[redacted]

School: [redacted]

Problem Definition

In developed countries, birth asphyxia affects 3-5 infants in 1000 live births, with 0.5-1 infants in 1000 live births developing brain damage in the form of hypoxic ischemic encephalopathy (HIE).[1] Data from developing countries suggests that the rate of HIE in infants is much higher, with an estimated 5-10 infants affected in 1000 live births.[1] Without treatment, infants affected by HIE have a 60% mortality rate. Infants who survive have a 25% chance of a significant handicap due to brain damage.[1]

Over the last decade, therapeutic hypothermia has been shown to reduce both the mortality rate and the prevalence/severity of brain damage in infants with birth asphyxia. The therapy works by lowering the temperature of the brain, which affects numerous pathways associated with neuronal cell death. A number of devices on the market in developed countries can effectively administer neonatal hypothermia therapy for prices ranging from $10,000-$20,000. These systems are very difficult to afford in low- and middle- resource settings.

In the past, there have been attempts to introduce low-cost methods for hypothermia therapy, including the use of fans in South Africa and the use of cold water bottles in Uganda. Unfortunately, these methods lacked the control necessary to stay safely within the therapeutic window. As a result, they were not nearly as effective as devices used in developed countries. In fact, the lack of control led to an increase of side effects, like coagulopathy and mortality.

Proposed Solution

We propose a low-cost, safe, and effective device for administering hypothermia therapy to neonates. Our device will provide hypothermia therapy localized to the brain for a period of 72 hours. The therapy will begin with a slow cooling period and end with a slow reheating period to ensure the infants safety. The device will monitor the infant's temperature, and the device will alter the therapy appropriately based on the infant's temperature. Furthermore, the device will be designed to have low initial and operating costs, and repairs necessary for the device will be possible with local equipment and expertise.

Through the use of our device, hospitals in resource-poor settings will be able to effectively administer hypothermia therapy for neonatal hypoxic ischemic encephalopathy (HIE).

1. http://apps.who.int/rhl/newborn/cd003311_ballotde_com/en/

Impact on Global Healthcare

Lowering infant mortality rates has long been identified as a very pressing need globally, with 99% of neonatal deaths occurring in low- and middle- resource settings. In response to this need, a number of campaigns and products have been launched over the past decade to reduce infant mortality rates in resource-poor settings. One program called the Helping Babies Breath (HBB) program is extremely relevant to our device.

The HBB program is a neonatal resuscitation curriculum for resource-poor settings. This program has been shown to effectively reduce the mortality rates of asphyxiated infants, but it is creating a secondary problem. As explained in the problem definition, asphyxiated infants are at a very high risk for developing hypoxic ischemic encephalopathy (HIE). As the number of asphyxiated infant mortalities is lowered with programs like the HBB, the number of cases of HIE will rise.

Our device is an essential component in providing care for asphyxiated infants. If hypothermia therapy is not available to resuscitated infants that suffered from birth asphyxia, they will be at a high risk for brain damage induced by HIE. Furthermore, as resuscitation techniques and technologies become more common in resource-poor settings, the number of infants in need of our device will continue to rise.

Our device will provide hospitals in resource-poor settings with a low-cost, safe technology that effectively administers hypothermia therapy. This technology will improve the standard of care for newborn asphyxiated infants, lowering the mortality rates and lowering the prevalence/severity of brain damage.

Device Description

The CryoCover system uses cool water and a temperature control system to keep the infant's head within the therapeutic temperature range for hypothermia therapy. The water is kept in a reservoir within the internal housing of the device. The water in the reservoir is maintained at the desired temperature using a thermoelectric cooling element. The thermoelectric cooling element is connected to both a cold plate and heat sink, and a fan that cools the heat sink. This set-up is simple, robust, and low-cost, while still providing effective treatment.

The water from the reservoir is pumped through PVC tubing that winds through a custom-printed polymer cap that is secured to the infant. The polymer cap is designed to be puncture-proof but still suitable for removing heat from the infant. The water is pumped through the cap, cooling the infant, and then returns to the reservoir.

To ensure the infant never gets too hot or too cold, the CryoCover uses a microcontroller that interprets data from a temperature sensor placed on the infant. The microcontroller

then communicates with the cooling element to adjust the water according to the infant's needs.

The therapy period lasts a total of 72 hours. The beginning of the therapy is a 15-minute "slow-cooling" period, and the end of the therapy is a 4-hour "slow-warming" period. The infant's temperature changes slowly in both of these periods to ensure the health of the infant. During the bulk of the therapy, the temperature control system tightly monitors the infant and water temperature to keep the infant within the therapeutic temperature range, which is a grey matter temperature of 33-34°C.

The final product will include an LCD display and LED indicators for displaying the infant's vital signs and progress through therapy to the caretaker. The device will only be used in the NICU, as patients undergoing this therapy require monitoring and are often suffering from other pathologies.

Final Prototype Design

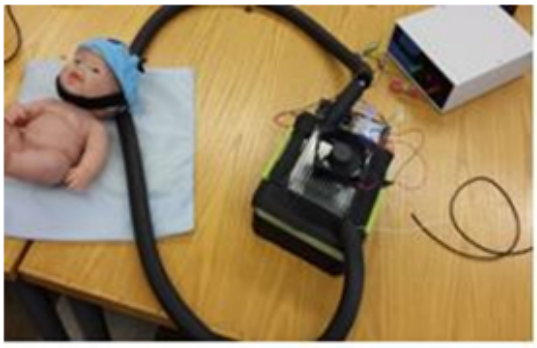


Figure 1: Entire CryoCover system connected to neonatal model

Figure 2: Custom-spiraled polymer cap

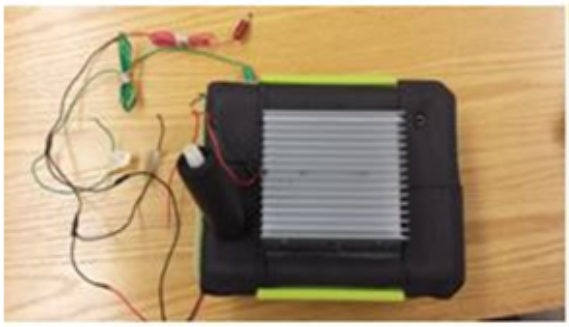


Figure 3: Water reservoir and TEC

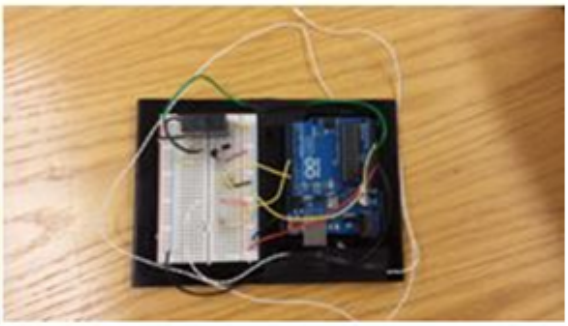


Figure 4: Thermistor and circuit

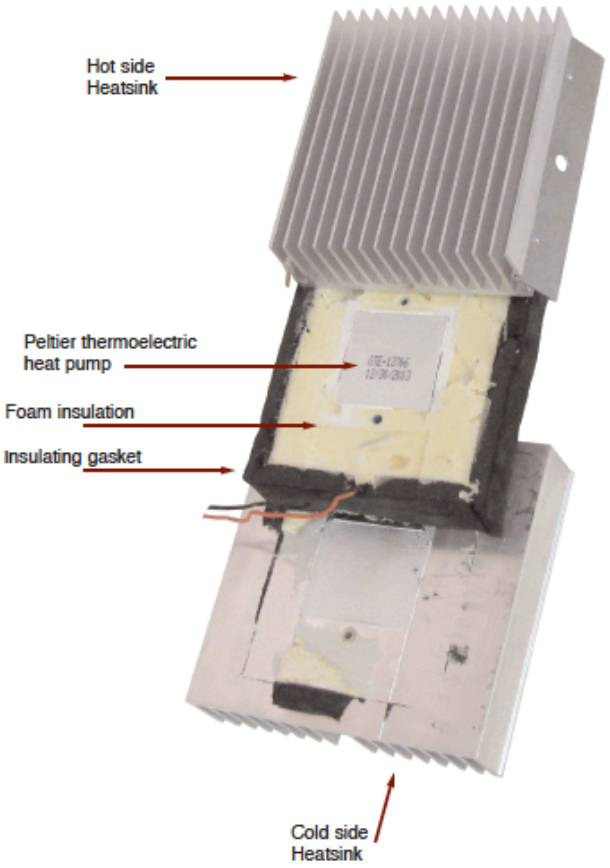


Figure 5: Thermoeletric cooling device courtesy of All Electronics Corp.

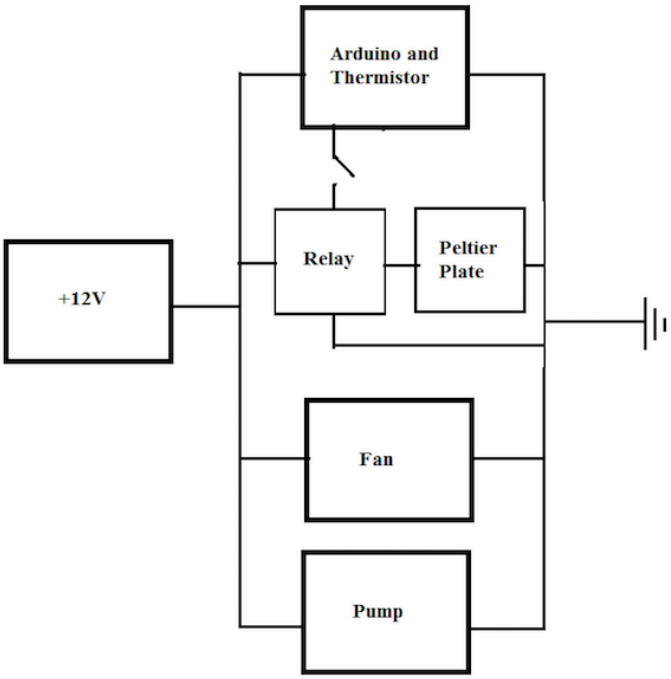


Figure 6: CryoCover circuit diagram.

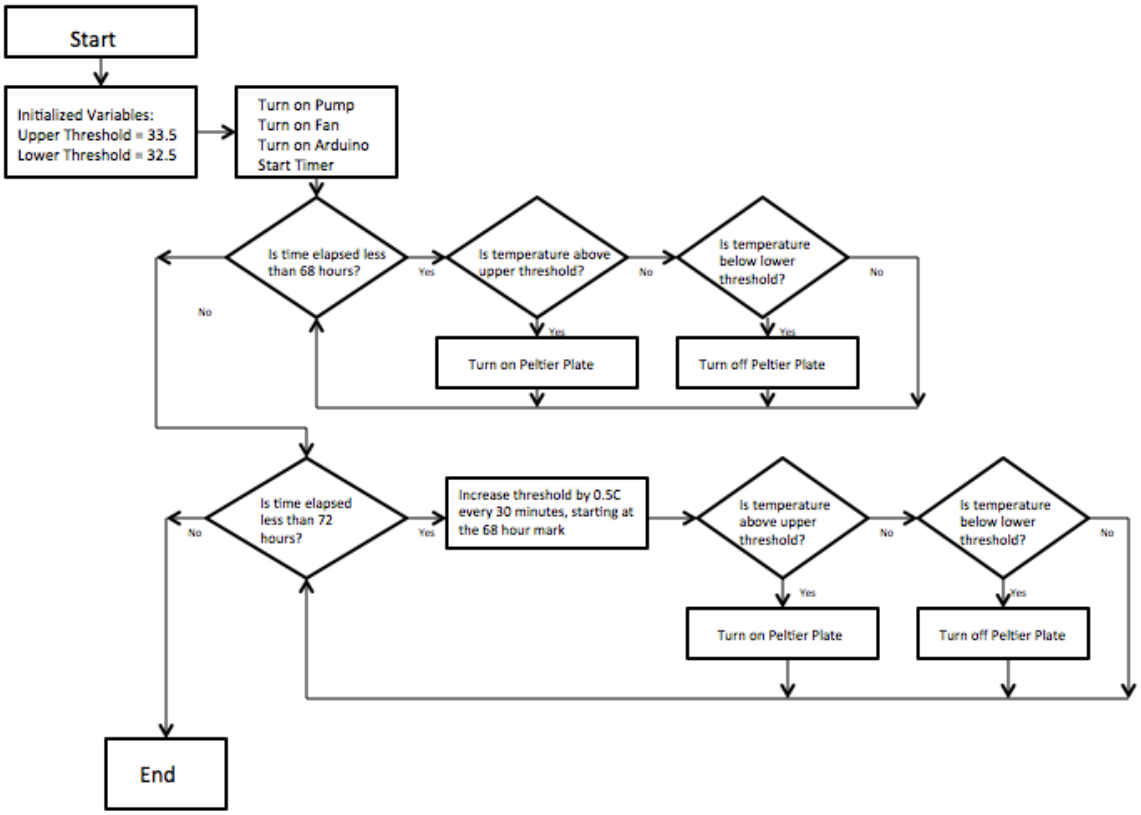


Figure 7: CryoCover circuit logic flowchart.

Cost of Device

For the production of each device, we must consider the raw and pre-made materials, labor for creating the contacting surface and insulation cap, machining of the coolant reservoir, as well as the sterilization, packaging and shipping of the device.

Gamma radiation sterilization was chosen because it is relatively inexpensive and the use of an autoclave is not feasible due to the use of incompatable plastics. In addition, only the shipping cost to get the device to the distribution center was taken into account. We did not consider the cost of shipping the device to the customer as this varies depending on the customer's location and it was assumed that a third party would perform this service at a separate charge to the customer.

Taking all of these factors into account, we have a total production cost of $335. Other expenses that will affect our final cost include the initial cost to creating a mold for the contacting surface, research and development as well as storage of the product after manufacturing. It is assumed that our device will not be sold in the United States, so we have not included costs to licence and sell the device in this location.

In addition, the cost of approval in other nations has not been listed because it can significantly vary based on our customer base. This would increase our initial cost and require a greater amount of devices to be sold before breaking even. We wish for our device to be affordable for hospitals without substantial funding, so we have decided on a final price of $700. This relatively low price will make our product appealing to our customers while still allowing us to generate enough profits to sustaine the company producing the product. We will have to sell approximately 160 devices to break even with our investments.

Device Testing

A number of tests were performed on this device. Verification tests were performed to ensure the power supply, pump, temperature probes, and tubing/cap interfaces were function properly. Verification tests were also performed to ensure that infant head size, head weight, and tubing positioning would not negatively affect the therapy. The data for these tests is not included here as all of the components performed without error, as no significant deviations from the control were shown.

The testing included herein addresses the most critical issue of this design project: will this device safely cool an infant's brain to the therapeutic temperature range of 33-34°C? To answer this questions, the following two tests were performed.

Test 1: COMSOL Model of therapeutic cooling through sagittal cross-section of an infant's head

Purpose: Model the cooling profile that the CryoCover could create when applied to a newborn infant.

Methods: To model the cooling profile of the CryoCover, a sagittal cross section of the CryCover device an infant's head were constructed in COMSOL. The cross section had the following layers: white matter, grey matter, skull, scalp, CryoCool cap. The material properties of each layer were determined from the literature. The parameters of density, thermal conductivity, specific heat, and arterial temeprature were constants, as they all have very low temperature-dependance. The parameters of metabloic heat and perfusion rate were functions of temperature, as they are highly temeprature-dependant. Human tissue started at body temperature (37°C) and water temperature was set to 12°C. The temperature in the grey matter was observed over time.

Results:

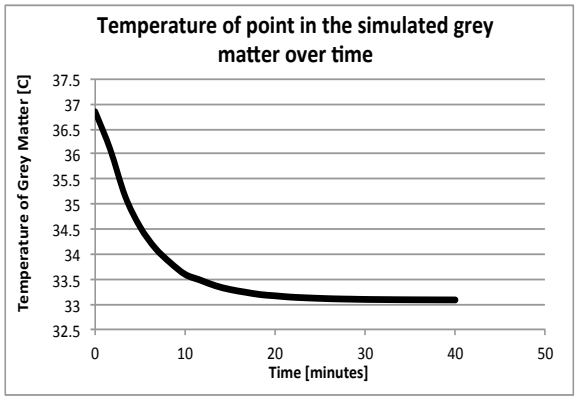


Figure 5: Change in temperature in the simulated grey matter over time.

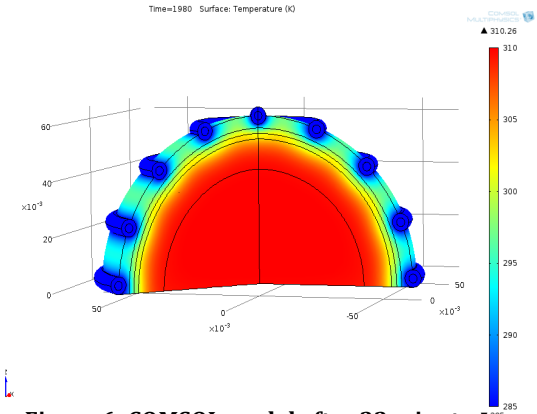


Figure 6: COMSOL model after 33 minutes when the system reached steady state.

After running for 40 minutes, the grey matter temperature reached 33.1°C. A plot of the change in time of the grey matter temperature for a representative point was recorded with a point analysis. Also, the thermal map of the infant's head after 40 minutes was recorded.

Conclusion: The CryoCover was shown effective in the model for lowering grey matter to the therapeutic range using 12°C water. However, a study of the physical device must be done to ensure the material properties of the cap and tubing were correctly simulated.

Test 2: A comparison of scalp-cap interface temperatures in both the COMSOL model and the physical prototype.

Purpose: To determine if the CryoCover model in COMSOL accurately depicts the prototyped CryoCover device.

Methods: To determine if the COMSOL model is accurate, a point analysis on the inner surface of the polymer cap in COMSOL For comparison, an NTC thermistor was used to monitor the temperature of the inside of the prototyped cap over as 12°C was pumped through the cap with our system. Data was recorded and plotted to observe the change in temperature over time for both the COMSOL and physical models.

Results: The COMSOL model showed a decrease to 13.8°C over 30 minutes, while the model showed an average decrease to 15.5°C over 30 minutes.

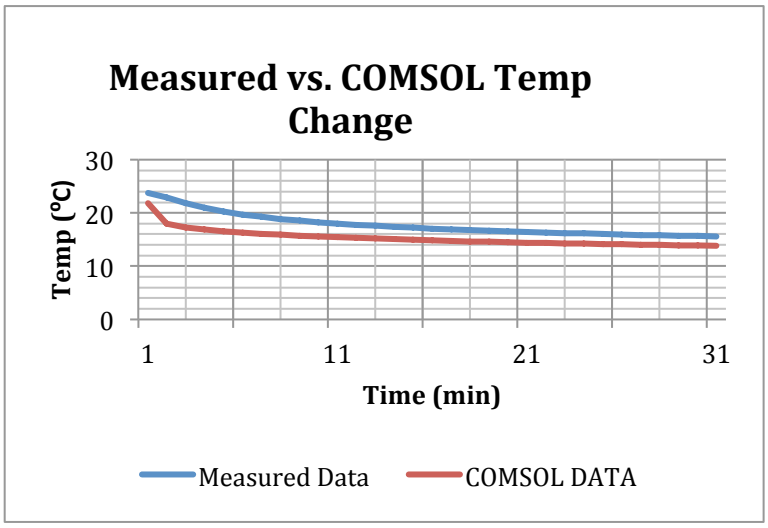
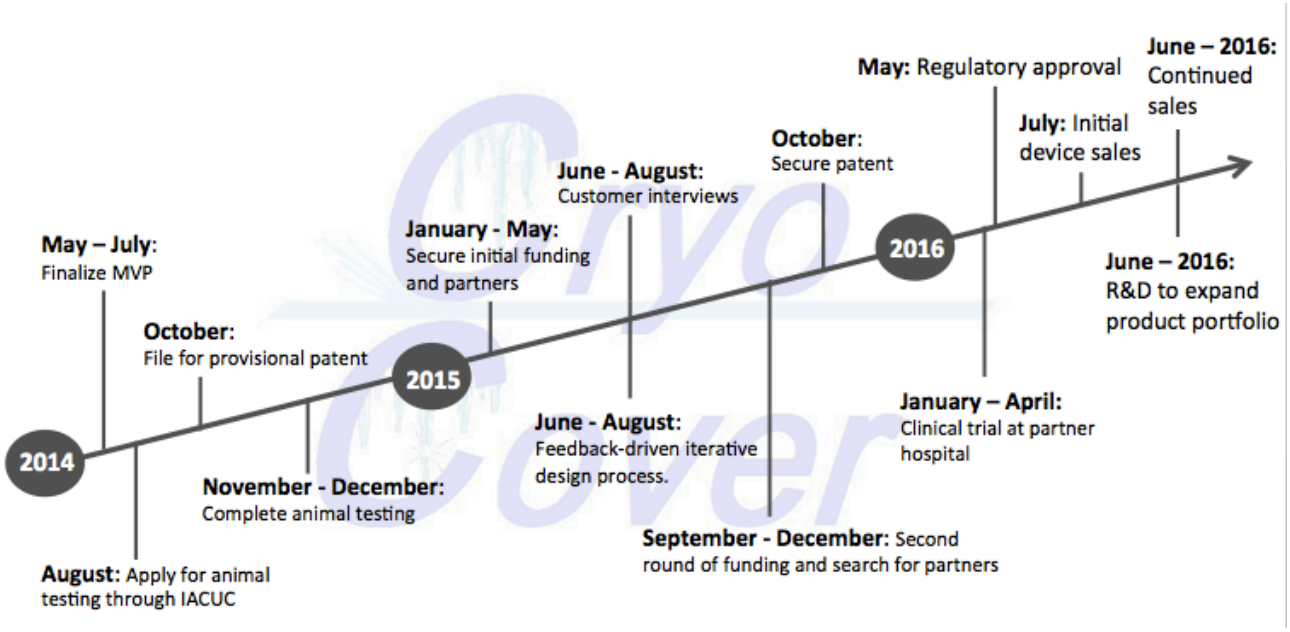


Figure 7: Measured cap temperature vs. COMSOL model temperature change over 30 minutes. n=3

Conclusions: While there was a 1.8°C difference between the COMSOL and physical models, it is believed that the difference can be overcome by cooling the water to a slightly lower temperature. Initial tests confirmed this finding in COMSOL, but time restrictions did not allow us to investigate in the physical model.

Commercialization Plan

Following is the commercialization plan for the CryoCover. The plan outlines a potential path to market for the device from now through distribution and sales. A VC firm will most likely be included in the commercialization process during the first or second round of investing (as noted in the timeline).



After the school year ends, research and development will be continued over the summer until a minimum viable product (MVP) is produced in July. Funding for this development will most likely be obtained through the university or the inventors. After the MVP is created and final verification testing is done, the team will apply for animal testing using a piglet model at Godley-Snell. Throughout the summer, the team will work with [redacted] to secure a provisional patent for the technology. Costs associated with IP will be covered by [redacted]. The team will complete the animal model after approval is given. All work up to this point will have been done through university facilities.

After the animal model is completed, the team will seek out initial capital, most likely through design contests or industry partners. With funding secured, the team will conduct three months of thorough customer interviews to gain a better understanding of the market and design needs of the end-game users and customers. Design modifications will be made throughout this process to best meet the needs of the customer.

After customer interviews are complete, the team will secure a second round of funding, either through new or existing partners. With this funding or through [redacted], the team will secure a patent for the technology. The team will then create an initial inventory of CryoCover systems and partner with a hospital to debut the CryoCover in a clinical trial.

After the clinical trial, the team will petition the US FDA for regulatory approval using a 510k pathway by demonstrating substantial equivalence to the Olympic Cool-cap System. US FDA approval is key because it will lead to quick regulatory approval in most countries. Going separately through the regulatory bodies in each target country could slow market entry. After

receiving FDA approval, the team will petition the regulatory bodies in target countries separately and begin device sales. Over time, the profit generated from sales will be used to pay back invested stakeholders and reinvest into the company through R&D that will expand the product portfolio.

According to the projections below, the company will break even after the sale of 160 CryoCover systems. Note that the overhead estimates and unit price used to make these projections both include service contract estimates for a 2-year warranty. It should also be noted that startup costs can be affected by through the "miscellaneous regulatory fees." These fees are meant to account for the cost of petitioning regulatory agencies in various countries. These fees can vary substantially based on the countries where devices are sold.

Startup Costs	
Overhead	$30,000
Continued R&D	$3,000
Manufacturing Facility	$10,000
Patent fees	$10,000
FDA 510k	$5,000
Misc regulatory fees	$3,000
Initial Inventory	$35,000
Startup Costs	**$96,000**

Cost Per Unit	
Materials	$225
Manufacturing	$75
Overhead	$400
Cost per unit	**$700**

Pricing Model	
Unit Cost	$700
Unit Price	$2,000
Profit Margin	**$1,300**