Therapeutic Hypothermia Saline Cooling Device

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Abstract

Research has proved that inducing hypothermia in post-cardiac arrest patients is an effective treatment to reduce the brain damage that results from ischemia and blood reperfusion. In Dane County, the method for inducing hypothermia in a post-cardiac arrest patient during transport to a hospital involves infusing chilled saline into the patient. Saline is stored in a refrigerator at the hospital and is placed in a soft-sided cooler with ice for transport to the patient's location. The main problem with this protocol is cooling the saline and keeping it cold, even when the ambient temperature is high. Optimally, the saline should be at a temperature of 4°C when it is infused into a patient. The cooler currently in use does not allow measurement of the temperature of the saline; it is suspected that the saline never reaches a temperature of 4°C. The goal of this project is to design a device that can be used to cool the saline and keep its temperature at 4°C during infusion. The device will be used in ambulances and helicopters so space constraints, as well as power availability, need to be considered. Possible cooling devices include thermoelectric coolers and miniature refrigerators. Options for insulating the saline bag and cooling the saline below 4°C will also be explored.

Problem Statement

To reduce the risk of brain injury and slow cerebral reperfusion in post-cardiac arrest patients, hypothermia is induced during helicopter or ambulance transport. Hypothermia is induced by infusing saline at 4°C to reach a core body temperature of 32°C to 34°C. To ensure that saline enters the body at 4°C, a method of cooling and maintaining the saline temperature is needed. The method must consider the space constraints of an ambulance or helicopter (figures 1 and 2). Alternative methods, including evaporative cooling, can be used in conjunction with cold saline to induce hypothermia more rapidly. Upon arrival at the hospital, methods are already in place to maintain hypothermia. For effective implementation in Emergency Medical Services nationwide, the method must be cost-effective.

Background

Post-Cardiac Arrest Brain Damage

Neurological damage is a common result in patients following cardiac arrest. Cardiac arrest results in a condition known as ischemia, which is marked by reduced or ceased blood flow to a particular organ or portion of the body. When dealing with a cardiac arrest victim, ischemia specifically refers to a lack of blood flow to the brain. This low flow state then leads to anoxic brain injury. Anoxic brain injury is caused by an insufficient supply of oxygen reaching the brain and results in damage to brain cells. Additionally, brain damage can arise in a victim post-cardiac arrest. This secondary brain damage is caused by reperfusion, the reintroduction of blood flow to the brain. The newly introduced blood flow brings oxygen to the brain which damages cellular proteins. Reintroducing oxygen to the brain damages plasma membrane proteins of the already damaged cells, causing them to rupture and release toxic free radicals into

surrounding cerebrospinal fluid. Free radicals act on neighboring cells, causing them to rupture and release more toxins. This leads to a never ending cascade of brain damage that will eventually result in death [1]. Recently, research has proven that inducing hypothermia in comatose post-cardiac arrest patients significantly slows this ischemic cascade and reduces neurological damage.

Therapeutic Hypothermia

The effectiveness of therapeutic hypothermia treatment has been clinically proven in two separate studies. Both studies were published in 2002; one took place in Australia while the other took place in Europe. Additionally, both studies used similar methods for comparing results between patients treated with hypothermia and patients treated with standard care procedures. Patients who were resuscitated after cardiac arrest were randomly assigned to undergo either therapeutic hypothermia or standard care procedures. In the European study, the primary endpoint was to see if a favorable neurological outcome occurred 6 months after treatment. The secondary endpoint was to see if death occurred within 6 months of treatment as well as determine the rate of complications within 7 days of treatment. In the group treated with hypothermia, 75 of 136 patients (55%) had a favorable outcome. In the standard care group, only 54 of 137 patients (39%) had a favorable outcome. Mortality in the hypothermia group at 6 months was only 41% as compared to 55% in the standard care group [2]. Similar results were seen in the Australian study. In the group treated with hypothermia, 49% of patients had a favorable outcome, whereas the group treated with standard care only had 26% of the patients experienced a favorable outcome [3]. A favorable outcome was described as a patient having minimal brain damage resulting in good cerebral performance or only slight disability. Favorable outcome patients were patients that were discharged from the hospital to their homes

or a rehabilitation center the next day. The results of both studies showed that inducing hypothermia increased the rate of good neurological outcome and reduced mortality. In general, inducing hypothermia increased survival rate, and more importantly, the quality of life after the occurrence of a heart attack.

Inducing Hypothermia Out-of-Hospital

Inducing hypothermia out-of-hospital is a fairly simple process that utilizes the effects of infused cold saline. In a typical patient, 2 L of saline are infused to induce hypothermia. The saline is infused during transport from the site of the cardiac arrest to the hospital. Transport is either by ambulance or helicopter. Transport takes an average of 20 – 25 minutes by ambulance and 35 minutes by helicopter. It typically takes 15 minutes to infuse 1 L of saline into a patient, so the rate of infusion necessary to adequately cool the patient is very rapid. The saline is infused at a temperature of 4°C in order to reach a core body temperature of 32°C – 34°C. A core body temperature of 32 – 34°C results in hypothermia.

In Dane County, the emergency protocol for inducing hypothermia is a very rudimentary process. At the hospital, a few bags of saline are stored in a refrigerator between cardiac arrest calls. When the ambulance or MedFlight helicopter crew receives a call for a cardiac arrest victim, they simply remove the saline from the refrigerator, stow it in a soft-sided lunch cooler with two ice packs, and take off. With the current protocol, the EMS crew does not know if the saline is at 4°C while it is in the refrigerator, let alone whether it is cold enough during transport or infusion.

Existing Devices

There are currently no devices on the market to induce therapeutic hypothermia in the field. The first research on out-of-hospital induced hypothermia was not published until 2007 and suggested that cooling the body with chilled-infused saline out of the hospital is safe and effective at reducing post-cardiac arrest brain damage [4]. Devices for inducing hypothermia in-hospital include the ArticSun® by Medivance and Celsius Control System™ by INNERCOOL. ArcticSun® is a set of pads filled with circulating temperature-controlled fluid that are placed on the patient. The pads cool the patient by thermal conduction [6]. The Celsius Control System™ utilizes endovascular cooling and involves inserting a catheter into the inferior vena cava. Cooled saline flows from a console through the catheter and exchanges heat with circulating blood. No fluid is infused into the body [7]. While both systems are suitable for hospital use, they are too large, have too many components and require too much power to be implemented in the field.

Product Design Specifications

The main function of this device is to cool and maintain saline at 4°C. The device should function effectively in ambient temperatures of up to 45°C. The device should keep saline at 4°C -8°C for at least 40 minutes in accordance with average helicopter and ambulance transport times. The device needs to be small enough to fit in the available space of a helicopter (figures 1 and 2). For patient and doctor safety, all components of the device will need to be secured in the helicopter or ambulance. Because the device will be used in the field, it should not rely completely on an external power source. The device also should not cool the saline below its freezing point. Because the device could be implemented county- or nationwide, manufacturing costs should be considered.

Preliminary Saline Testing

Preliminary tests were performed to characterize the saline temperature changes and flow rate. This test also served to develop better methods for future testing. The 1 L bag of saline was cooled to 4˚C. It was hung from a hook approximately 4 feet above the ground. Standard 16 gauge medical tubing was attached to the bag. The end of the tubing was placed in a beaker on the ground (approximately 4 feet below the bag). Temperature probes were placed in the bag and in the beaker to monitor the temperature change as the saline flowed out of the bag. The saline was allowed to run freely through the tubing and temperature readings were taken every 30 seconds. The results are summarized in the graph below (figure 3).

As expected, the temperature of the saline in the bag increased exponentially (approximately +3˚C in 6 minutes). The temperature in the beaker remained somewhat constant. The constant beaker temperature was unexpected and is most likely due to the slow thermometer response time and the difficulty of taking accurate temperature measurements at the tip of the tubing. This will be improved in later testing by using a thermistor rather than a thermometer. This test established that the saline bag will need to be insulated to prevent warming.

A second test was conducted to find a method to slow the flow of saline to mimic the time it takes to infuse 1 L of saline into the human body. The MedFlight crew reported an approximate rate of infusion of 1 L every 15 minutes. Running the bag of saline through the tubing alone provided a flow rate of 1 L every 6 minutes. To slow the flow of saline, the tubing was modified by attaching a 16 gauge needle, similar to the one used to place an IV into a patient. This slowed the saline flow rate to approximately 1 L every 14 minutes, very close to the desired 1 L every 15 minutes.

Design Alternatives

Five alternatives were developed for cooling and maintaining the temperature of the saline during transport to the site. The first three alternatives involve portable coolers or refrigerators to cool the saline. The last two options address the issue of maintaining a chilled temperature.

Saline Cooling Alternatives

The first design utilizes an upgraded version of the soft-sided cooler currently used by the MedFlight crew. This option is advantageous because it is smaller and lighter than the other two coolers being considered and does not require an outside power source. A major disadvantage of this design is that there is no control of the temperature. The saline would probably maintain a reasonable temperature in the winter, but in the summer with higher ambient temperatures, the saline will warm much more quickly. This design can only be implemented if the method (described below) for insulating the saline bag is effective at keeping the saline cold for extended periods of time.

The second cooler being considered is a thermoelectric cooler. It operates on the Peltier effect where a voltage difference is converted to a temperature difference. A current is run through two different conductive materials with different electron densities. As the electrons move from the higher density material, the electrons expand and cool which creates a temperature difference [8]. This design allows for some temperature control. A disadvantage of this design, however, is that it works on a temperature differential with a maximum cooling ability of about 40˚ F below the ambient temperature. This means that if the temperature outside is 32˚C (90˚F), the temperature in the cooler could only get down to 10˚C (50˚F), which is not low enough to keep the saline at 4˚C. These coolers can be very small, so it would fit in the

helicopter and be easy to transport. Thermoelectric coolers are available commercially for $50 - $100.

The third cooler is a miniature refrigerator. The major advantage of this design is that the temperature can be set anywhere between -18˚C and 5˚C. A refrigerator, however, requires a power source and would be heavier than the other two design options. The refrigerator would most likely be a permanent fixture in the helicopter. Although there are refrigerators small enough to fit in the helicopter, the MedFlight crew may not want it to permanently take up space because they do not respond to cardiac arrest victims on a daily basis. Refrigerators smaller than 20 in x 20 in x 20 in are available commercially for $100-$250.

Saline Temperature Maintenance Options

In addition to implementing a device that will cool the saline bag during flight, a means of keeping the saline cold is also needed. One way to do this is to insulate the bag of saline with a sleeve. This sleeve would be slid over the bag of saline and fixed there. It will be kept around the bag while it is in the external cooling device. This sleeve will consist of an insulating material with pockets for removable ice packs (figure 4). Possible insulating materials include neoprene, often used in beverage "cozies" [9], or insulated mailing envelopes.

Insulating the tubing may also be an option. This, however, presents a challenge because the straight length of tubing is an awkward shape to cover. The physician also requires access to certain points on the tubing which means the insulation could not be one continuous cover. An easier way to insulate the tubing might be to coil the excess length in the middle and cover the coil as a whole. A flow rate test with coiled tubing showed that this had no dramatic effect on the rate of flow of saline through the tubing.

A second way to ensure that the saline stays chilled until it enters the body is to cool the saline below 4˚C but still above the freezing point of saline. As the saline warms during infusion, the temperature will rise to 4 ˚C. Saline cooling tests are needed to determine the freezing temperature of saline.

Decision Matrices

Two decision matrices are shown in appendix B. For matrix 1, only the three cooler alternatives were evaluated. The other two options, insulation and extra cooling, will be implemented in conjunction with a cooler if they are found effective; these results will ultimately affect the choice of cooler. When the effects of insulating the bag were ignored, the miniature refrigerator scored the highest. This design is the best for temperature control, which was the most highly weighted element. If an insulation sleeve successfully keeps a chilled bag of saline cold, temperature control becomes less important and size, cost and required power become more important. In this case, a standard soft-sided cooler is most likely the best option (see matrix 2).

Final Design

After considering all options, we decided to pursue a design that involved insulating the bag and tubing with neoprene sleeves. If successful, this will eliminate the need to purchase an expensive refrigerator that would most likely take up too much space in the helicopter or ambulance. The soft-sided cooler and ice packs currently used by the MedFlight crew will be used in conjunction with this design.

Prototype Design

An insulated sleeve was constructed to cover the bag of saline (figure 5). The sleeve is 6 inches wide by 11 inches tall. It is made of neoprene, the material used in wetsuits. It has Velcro to close the top of the sleeve, and a Velcro pouch on the back to hold a small ice pack. There is an opening at the bottom of the sleeve to allow the user access to the saline bag.

A pouch was constructed to insulate the coil of tubing (figure 5). Two pouch styles were created to insulate the tubing. The first pouch is circular and 3 inches in diameter. The opening at the top is secured with Velcro. The second pouch is the same shape as the first but slightly larger with a diameter of 5 inches. The extra space is for an ice pack if extra cooling throughout the tubing is deemed necessary. For both pouches, the user can coil the tubing around his/her hand and place the coiled tubing in the pouch. This strategy allows the user access to all necessary valves, while still insulating most of the tubing.

The materials for the sleeve and the pouch combined included the cost of the neoprene, needle, thread, and Velcro. This totaled approximately $20.

Prototype Testing

Testing was performed on the insulating device to ensure that it successfully reduced the heat transfer to the saline in the bag and during flow through the tubing. The first test performed was to verify the insulating capabilities of the neoprene. Thermometers were inserted into two bags of saline. The first bag was encased in the insulating sleeve, and the second was out in the open. The temperature in each bag was taken every minute. The ambient temperature in the room was 28˚C. Figure 6 shows that the temperature in the uninsulated bag increased more rapidly than the temperature in the insulated bag. The temperature increased linearly over time because no saline was flowing from the bag. The insulated bag increased from 2˚C to 3.5˚C over

15 minutes whereas the uninsulated bag increased from 3˚C to 7.5˚C. This test demonstrated that the insulating capabilities of the neoprene were sufficient.

A second test was performed to determine the insulating capabilities of the sleeves for the saline bag and the tubing while saline was run out of the bag. Again two sets of saline and tubing were used: one was insulated with our device and the other was left uninsulated. The test was carried out at an ambient temperature of 28˚C. Saline was run from each bag through the tubing. The temperature of the saline in the bag and the temperature at the end of the tubing were recorded every minute. The graphs of temperature over time for the insulated and uninsulated systems are shown in figures 7 and 8. The temperatures of these tests increased exponentially over time because saline was flowing out of the bag. The saline at the exit of the tubing followed the same exponential curve as the bag because there was a finite amount of heat transfer to the saline through the tubing that was not dependent on the amount of saline in the bag. The initial temperature of the saline exiting the insulated tubing was lower than uninsulated tubing, and the temperature increased at a slower rate. This shows that the tubing insulation is successful in eliminating some heat transfer to the saline in the tubing. The final temperature in the uninsulated bag was 13˚C and the final temperature for the insulated bag was 8.5˚C. Since both bags started at the same temperature and ran for the same amount of time, the insulating sleeve is successful in preventing heat transfer to the saline in the bag.

Some inaccuracies could have resulted because of the difficulty to get an accurate temperature at the exit of the tubing. Since a thermometer was used, it was difficult to cover the whole tip of the thermometer in the flowing saline. Also, errors could have occurred with reading of the thermometers. These tests will be repeated to ensure accuracy and to reduce variability.

Safety and Ethical Considerations

The main safety concerns with this device are cooling the patient to a core body temperature less than 32˚C and infusing crystallized saline. While inducing hypothermia, EMS carefully monitor the patient's body temperature to prevent excessive cooling. To prevent saline crystallization, the saline should be stored at a temperature no colder than 0˚C. All components of the device will also be strapped down in the helicopter and ambulance.

Future Work

Over the course of the semester, our team has been able to build and test a prototype that maintains a low enough saline temperature to successfully induce hypothermia. However, if we choose to continue this project in future semesters, there are a few aspects our team would like to work on. Initially, we would like to build a few more prototypes and give them to our client. Ideally, our client will use our prototype over the course of the summer and give us feedback on how well it did or did not work. Based on this feedback, the prototype would be tailored to better meet our client's needs.

We would also like to perform additional tests in the following semester. Testing our prototype in the winter made it very difficult for us to test in ambient temperatures that mimic the high temperatures experienced in the middle of summer. We would also like to run several tests with an icepack in the insulating sleeve, and if possible, the tubing sleeve as well. Most importantly, we would like to repeat all tests numerous times to get repeatable data and reduce variability. Should repeated testing produce consistent data and we receive positive feedback from our client, we would like to pursue a patent for our product and finalize manufacturing specifications of our design.

References

[1] Richmond, T.S. 1997. Cerebral Resuscitation After Global Brain Ischemia: Linking Research to Practice. *AACN Critical Issues* [online], **8** (2)

[2] Bernard, S.A., *et al.* 2002. Treatment of Comatose Survivors of Out-of-Hospital Cardiac Arrest with Induced Hypothermia. *New England Journal of Medicine,* **346** (8): 557-563.

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[4] Kim, F., *et al.* 2007. Pilot Randomized Clinical Trial of Prehospital Induction of Mild Hypothermia in Out-of-Hospital Cardiac Arrest Patients With a Rapid Infusion of 4˚ C Normal Saline. *Circulation*, **115** (24): 3064-3070.

[5] Kim, F., *et al.* 2005. Pilot study of rapid infusion of 2L of 4 degrees C normal saline for induction of mild hypothermia in hospitalized, comatose survivors of out-of-hospital cardiac arrest. *Circulation*, **112** (5): 715-719.

[6] Medivance, Inc. 2007. http://www.medivance.com.

[7] INNERCOOL Therapies. 2007. http://www.innercool.com.

[8] Winder, J.W., Ellis, A.B., Lisensky, G.C. 1996. *Journal of Chemical Education,* **73** (10): 940.

[9] Silbert, C.E. 2001. *Neoprene bottle insulator.* US patent 6,550,271.

Appendix A: Figures

Figure 1: MedFlight helicopter, back

Figure 1. This is where the stretcher is loaded into the helicopter. There is some storage space on the right, but it would not be accessible during flight.

Figure 2: MedFlight helicopter, front

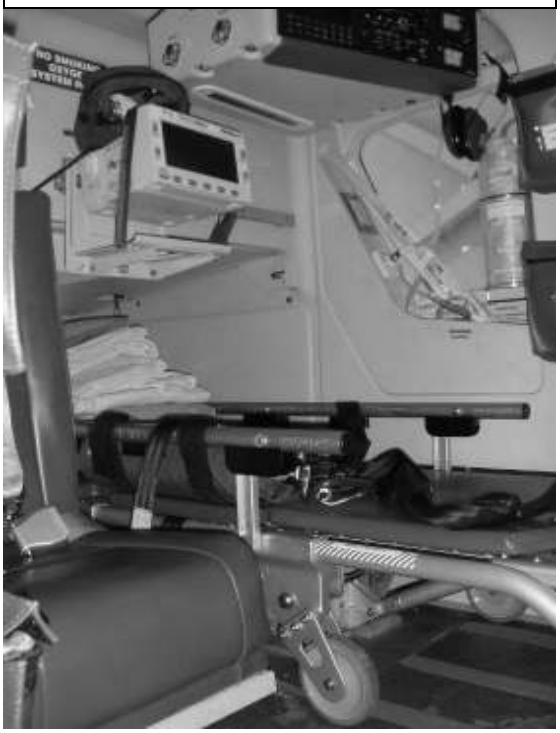

Figure 2. This is where the doctor and flight nurse work on the patient. The patient is accessible from the hips up. The saline bag is hung next to the monitor (top left).

Figure 3: Saline Temperature Change Over Time

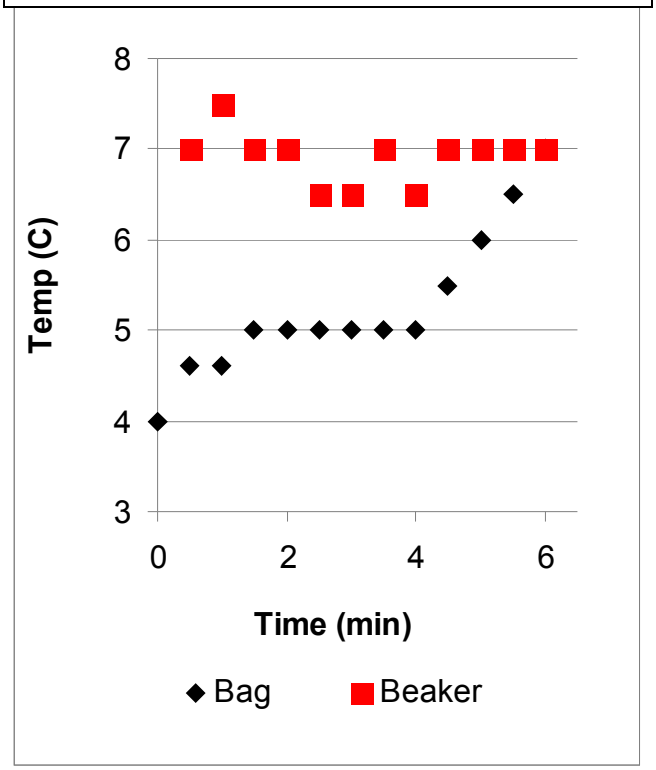

Figure 3. This graph shows the temperature of the saline in the bag and the saline in the beaker during a 6 minute temperature test. Readings were taken every 30 seconds and recorded in degrees Celsius.

Figure 4: Saline Insulation Sleeve
This picture is of the insulated sleeve containing ice packs (shown in green) which surround the bag of saline (shown in blue). The sleeve leaves an opening at the top to hook the bag.

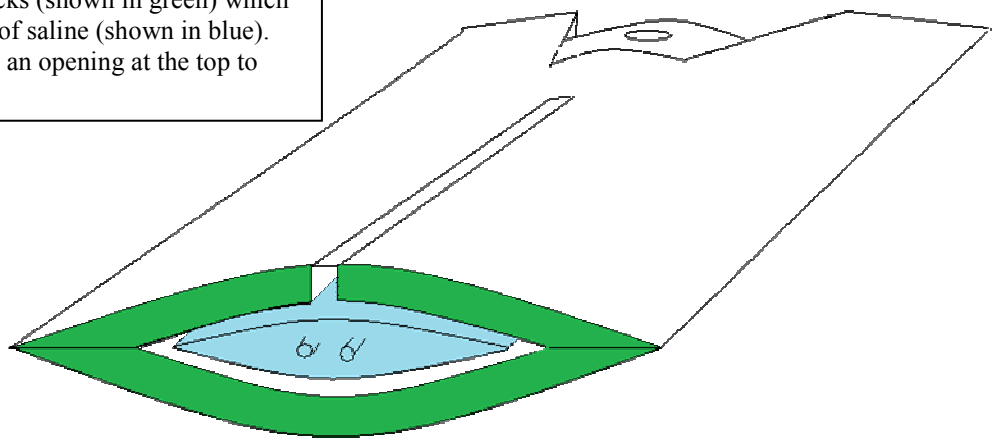

Figure 5: Constructed Prototype

Figure 5. The neoprene insulation sleeve is shown on the left. The tubing insulation pocket is on the lower right.

Figure 6: Insulated vs. Uninsulated Saline Bag Test

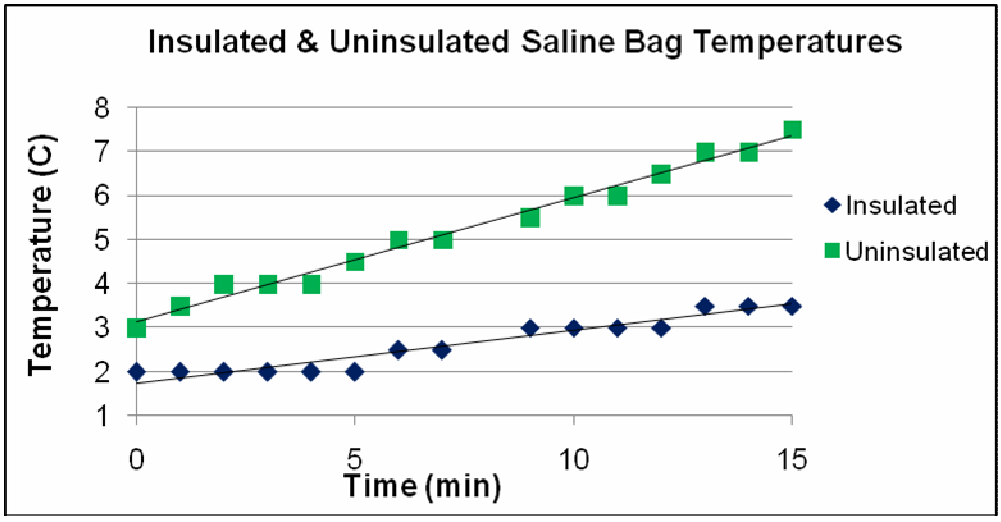

Figure 6. This test established the effectiveness of neoprene as an insulator. Over a 15 minute time period, an uninsulated bag of saline warmed more rapidly than a bag of saline insulated with neoprene.

Figure 7: Unisulated System Test

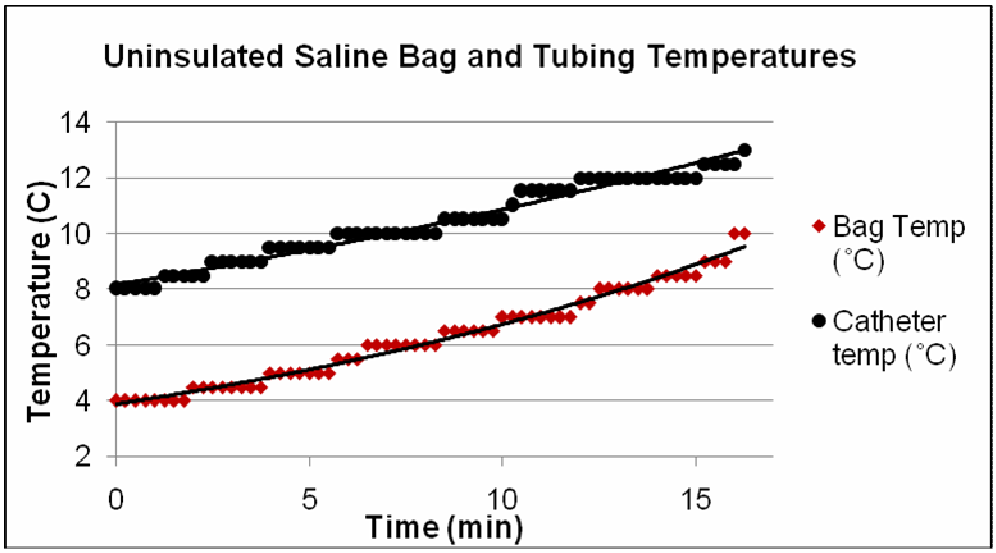

Figure 7. This test was performed with no insulation covering the bag of saline or the tubing. The ambient temperature was 28°C.

Figure 8: Insulated System Test

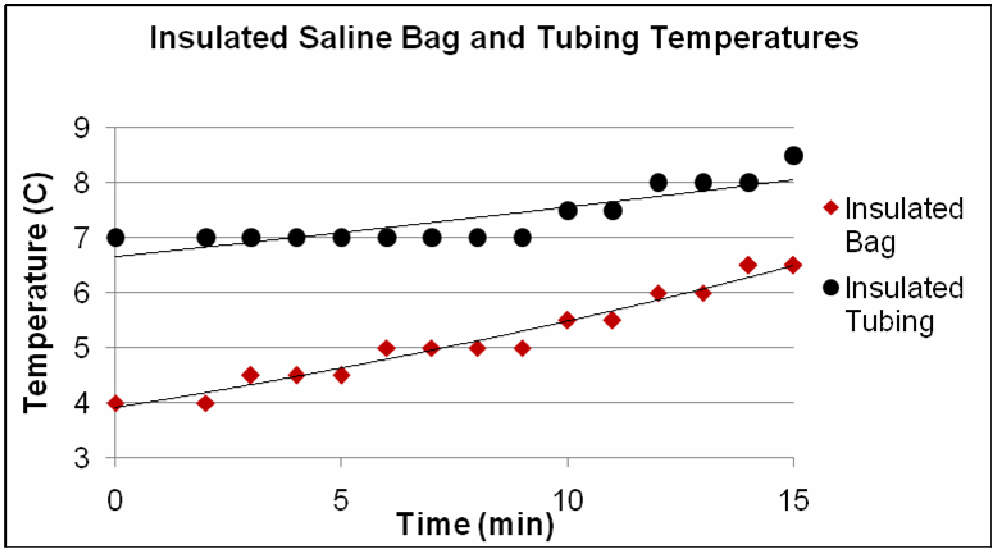

Figure 8. This is the same test as figure 6, but in this case the bag of saline and tubing were insulated with our device. The saline warmed more slowly when the system was insulated.

Appendix B: Decision Matrices

Matrix 1: Implementation of Insulation *Not Considered*

Criteria	Weight	Standard Cooler	Thermoelectric Cooler	Miniature Refrigerator
Cooling Ability	**0.40**	1	2	3
Size	**0.20**	3	2	1
Power Required	**0.10**	3	2	1
Client Preference	**0.20**	1	2	3
Cost	**0.10**	3	2	1
Total	**1.00**	1.8	2.0	2.2

Matrix 2: Implementation of Insulation *Considered*

Criteria	Weight	Standard Cooler	Thermoelectric Cooler	Miniature Refrigerator
Cooling Ability	**0.20**	1	2	3
Size	**0.30**	3	2	1
Power Required	**0.15**	3	2	1
Client Preference	**0.20**	1	2	3
Cost	**0.15**	3	2	1
Total	**1.00**	2.2	2.0	1.8

Appendix C: Product Design Specifications

In-Flight Patient Cooling Device

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May 5, 2008

Function: To reduce the risk of brain injury and slow cerebral reperfusion in post-cardiac arrest patients, hypothermia is induced during helicopter or ambulance transport. Hypothermia is induced by infusing saline at 4°C to reach a core body temperature of 32°C to 34°C. To ensure that saline enters the body at 4°C, a method of cooling and maintaining the saline temperature is needed. The method must consider the space constraints of an ambulance or helicopter. Alternative methods, including evaporative cooling, can be used in conjunction with cold saline to induce hypothermia more rapidly. Upon arrival at the hospital, methods are already in place to maintain hypothermia. For effective implementation in Emergency Medical Services nationwide, the method must be cost-effective.

Client Requirements:

- Fit in space available in medical transport vehicle (helicopter or ambulance)
- Easily transported
- Saline temperature maintained between 4-8°C
- Cool patient to a core body temperature of 32°C to 34°C
- Cost effective

Design Requirements

1. Physical and Operational Characteristics
    a. *Performance Requirements:* The device must cool the saline to 4°C and maintain this temperature as the saline enters the body. The patient should be cooled to a body temperature of 32°C to 34°C.
    b. *Safety:* Since the device will be used in transport, there should be no loose pieces. All components of the device must be able to be strapped down in the helicopter. Also, the patient's body temperature should not be cooled below 32°C and the saline should not be cooled to the point of crystallization.
    c. *Accuracy and Reliability:* The device must be able to maintain the saline at 4-8°C for up to 35 minutes. The saline should be as close to 4-8°C as possible as it enters the body.
    d. *Life in Service:* The device should be reusable and should function for at least 35 minutes without loss of function.
    e. *Shelf Life:* Not applicable at this time.
    f. *Operating Environment:* The device should function in ambient temperatures up to 45°C and high heat indices. The device must withstand frequent transport from the storage location to the ambulance or helicopter. It must also function in a moving vehicle. The device should not rely on power from an electrical outlet.
    g. *Size:* The device must fit in the limited workspace of an ambulance and helicopter.
    h. Weight: The device must be carried by paramedics. It should not weigh more than 30 pounds, but a lighter device would be more desirable as components may be placed on a patient while the stretcher is being loaded into the helicopter/ambulance.

i. *Materials:* The materials used should be durable, non-toxic, and easily sterilized.

2. Production Characteristics
    a. *Quantity:* One unit per ambulance and one unit per helicopter for Dane County Emergency Medical Services will need to be produced.
    b. *Target Production Cost:* Cost must be affordable for the Dane County EMS.
3. Miscellaneous
    a. *Standards and Specifications:* All components of the device must be secured in the helicopter or ambulance.
    b. *Subject-Related Concerns:* The device should not cool saline to the point of crystallization to avoid possible patient complications. Hypothermia should be induced as rapidly as possible.
    c. *Competition:* Other devices are currently on the market to induce hypothermia; however, they are not cost effective. The current method for cooling saline in Dane county is ice in a cooler.
        - Arctic Sun Temperature Management System® by Medivance - pads filled with temperature controlled water applied directly to the patient's skin, cools by thermal conduction (http://www.medivance.com/html/Products/etp.html)