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Evaluation of an Interstitial Cooling Device for Carotid Arterial Cooling Using a Tissue Equivalent Gel Phantom

In this study, we build and test a prototype of an interstitial cooling device in a tissue-equivalent gel phantom mimicking the human neck. The effectiveness of the device is measured by the capability of delivering a coolant temperature of lower than 5°C at the entrance of the device and the measured temperature decay along a glass tube filled with water circulating at a speed similar to that in the carotid artery. The experimental study has identified a cooling prototype design, which is capable of inducing sufficient temperature reduction along the common carotid artery. It also tests how easy to handle the device to ensure a close physical contact between the device and the glass tube. A 5°C coolant temperature can be delivered at the device entrance when using above 0°C coolant in the reservoir. The surface temperature of the device is found almost uniform. Despite its limitations, the experimental results agree generally with previous theoretical predictions. The 8 cm long and 3 cm wide device with a coolant temperature lower than 10°C is capable of inducing a temperature reduction of at least 2.5°C along the glass tube filled with water circulating at 240 ml/min. For higher water flow rates, one needs to increase the length of the device and/or lower the coolant temperature to achieve similar temperature decays along the glass tube. [DOI: 10.1115/1.4002196]

Keywords: brain hypothermia, cooling device, carotid artery, temperature reduction, gel

1 Introduction

In recent years, mild or moderate hypothermia during which brain temperature is reduced to 30–35°C has been proposed for clinical use as an adjunct for achieving protection from cerebral ischemia during cardiac bypass injury, carotid endarterectomy, and resection of extra-cranial aneurysm, as well as stroke and traumatic brain injury [1–4]. It has been shown that a reduction in brain temperature, as small as 2°C, substantially reduced ischemic cell damage [5] or improved significantly post-ischemic regional histopathology [6]. The major challenge facing the clinicians is to develop a cooling approach for achieving safe and rapid neuroprotective hypothermia while minimizing severe systemic complications.

Most clinical studies have examined only systemic hypothermia by whole body cooling. The major methodological drawback of this approach is a slow cooling rate (~ 0.5 deg/h) due to the large volume of the human body and arteriovenous shunt vasoconstriction [4,7,8]. Another limitation associated with whole body cooling is systemic complications, such as metabolic, cardiovascular, pulmonary, coagulation, and immunologic complications. The systemic risks may outweigh the beneficial effects of neurohypothermia in the current clinical practice.

Selective brain cooling, which keeps the rest of the body at normal temperature, on the other hand, can be used to maximize the neuroprotection of hypothermia. Most of the current commercial devices of selective brain cooling in the market are neck collars and head helmets. Recent theoretical [9,10], animal [11–16], and clinical [17] studies have demonstrated the feasibility of cooling the brain cortex via head surface cooling; however, it is unable to cool deep brain tissue. Using neck surface, one finds that the large thermal resistance of the neck muscle results in ineffectiveness of those devices when deep penetration and fast cooling are critical to the patient's outcome.

Our group has investigated an interstitial cooling plate for target cooling of the carotid arterial blood supplied to the brain tissue. The hollow cooling plate is made of flexible materials and can be inserted into the neck muscle and placed on the surface of the common carotid artery. The approach can greatly decrease the thermal resistance by ensuring a close physical contact between the flexible hollow cooling plate and the arterial blood. It is feasible in clinical applications, such as open surgical repairs in open heart and neck surgeries, when the accessible carotid artery has already been exposed. According to a previous theoretical study [18], the advantages of the proposed flexible cooling hollow plate are its small size (7×1 cm^2), powerful cooling capacity (~ 90 W), and fast cooling capability (<30 min). The cooling capacity of the device is directly proportional to the length of the device; however, it is insensitive to the device width. Experimental studies have also been performed in small animal models using a prototype of this approach [19,20] to monitor the temperature reduction in rat brain, as well as to investigate how the infarct volume in the brain tissue is decreased by the cooling. Both have demonstrated the feasibility and efficacy of this approach in small animal models. However, the cooling extent observed in the animal studies cannot be directly applied to human brain due to the difference of the head size between rats and humans.

In this study, we develop a prototype of the interstitial cooling device that has the potential to be used in clinical or large animal study. A glass tube mimics the common carotid artery in the human neck, and it is inserted into a tissue-equivalent agarose gel phantom to simulate heat exchange between the artery and the neck muscle tissue. The device's cooling capability is measured by temperature decays inside the glass tube filled with circulating water of 37°C at its entrance. The device is tested to evaluate the

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Contributed by the Heat Transfer Division of ASME for publication in the JOURNAL OF THERMAL SCIENCE AND ENGINEERING APPLICATIONS. Manuscript received March 11, 2010; final manuscript received June 23, 2010; published online September 9, 2010. Assoc. Editor: Lisa X. Xu.

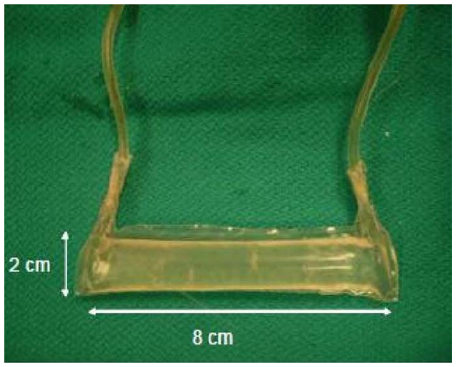

Fig. 1 A prototype of the cooling device made of polyethylene sheet and Teflon tubes

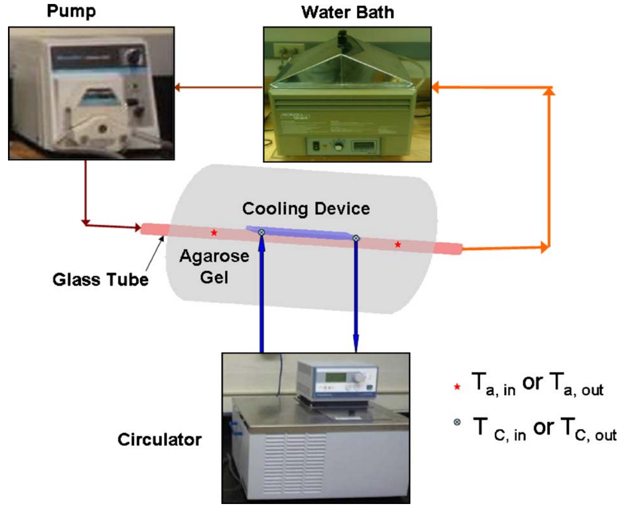

Fig. 3 Experimental setup consisting of a water reservoir, a pump, a cylindrical gel block, a glass tube, a circulator, a cooling device, and connecting tubes. Several thermocouples are used to measure temperature changes along the glass tube and in the cooling device.

ease with which the physical contact between the device and the glass tube can be ensured. The effects of different parameters on the cooling capacity of the interstitial device are also studied.

2 Materials and Methods

2.1 Cooling Device. Transparent polyethylene (plastic sheet) is used as the device material. The plastic sheet is flexible and can be easily used to assemble the prototype by a heat sealer. The finished prototype (8 cm long) is seen in Fig. 1 where the coolant flows in and out of the device from the two sides of the device. We have three prototypes devices of different widths (1 cm, 2 cm, and 3 cm). A rigid Teflon tube with an outer diameter of 5 mm is inserted into the cooling plate. Water serves as the coolant and is circulating through the cooling device via a circulator (Programmable Model 9012, PolyScience, Niles, IL). The circulator can heat or cool the coolant to a preset temperature ranging from −50°C to 99°C. Subzero °C coolant can be achieved by adding salt to water to maintain its liquid state. Using saline (5% NaCl concentration) is also preferred in future clinical or animal studies to ensure safety to the tissue in case of leaking. The flow rate of the coolant can be adjusted by the circulator to achieve a temperature at the cooling device entrance ranging from 5°C to 20°C, which is similar to the previous theoretical simulation analyses [18]. The coolant flow rate is set to 1000 ml/min in order to achieve a minimum coolant temperature of 5°C when the refrigeration system was set at 1°C. The inserted Teflon tubes are sealed at both ends of the hollow plastic device. The coolant inlet and outlet at the locations of the Teflon tube are sealed using glue and surgical suture.

2.2 Neck Model. A tissue equivalent phantom gel (3% agarose powder) is chosen and is prepared by dispersing agarose powder (Sigma-Aldrich, Saint-Louis, MO) in a 10% buffer solution (tris-borate ethylenediamine tetra-acetic acid (EDTA), Gibco BRL, Rockville, MD). The mixture is then heated until the agarose is completely dissolved. After being cooled at room temperature to 60°C, the solution is loaded into a cylindrical container and cooled further to room temperature (25°C) until solidification. A glass tube of 5 mm in diameter and 15 cm long is inserted into the center of the cylinder to represent the carotid artery before the agarose solution is poured into the container. The cylindrical container is 12 cm long and 12 cm in diameter similar to a typical size of a human neck, as shown in Fig. 2. Water is again used to simulate arterial blood flowing in the carotid artery. Figure 3 shows the schematic diagram of the experimental setup. Warm water at 37°C is pumped from a water reservoir maintained in a temperature controlled water bath. The water flow rate in the glass tube can be adjusted to achieve a flow rate of 240 ml/min, 360 m/min, or 480 ml/min, which covers the wide range of the blood flow rate in the common carotid artery [18,21,22].

2.3 Temperature Measurements. Four fine thermocouples (copper-constantan, 50 μm diameter wire) are used to evaluate the performance of the cooling device and the capability of the circulator to maintain a cold plate surface contacting the glass tube. As shown in Fig. 3, one thermocouple ($T_{c,\mathrm{in}}$) is inserted

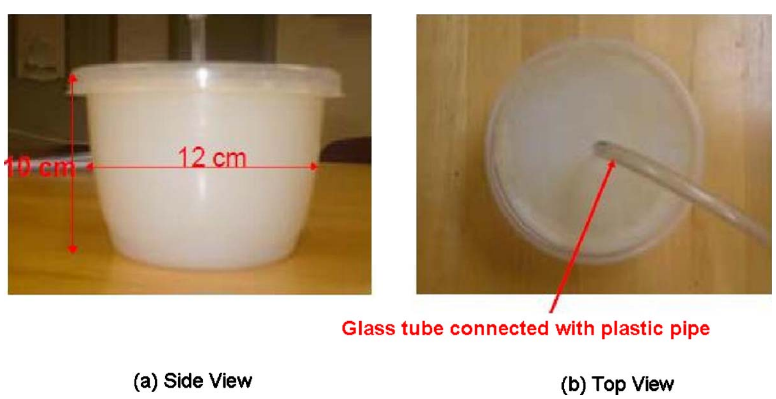

Fig. 2 Tissue equivalent agarose gel in a cylindrical container mimicking the human neck

inside the glass tube to measure the temperature at the inlet of coolant from the circulator. Another one is inserted to measure the temperature inside the Teflon tube at the outlet of the cooling plate ($T_{c,\mathrm{out}}$). The coolant temperature inside the cooling plate is calculated by the average temperature at its inlet and outlet. The outer surface temperature of the cooling plate is not measured in the experiment due to the large temperature variation on the surface in contact with the warm glass tube.

The cooling efficacy of the cooling plate is evaluated by the temperature decay along the glass tube. Two thermocouples are inserted into the glass tube to measure the inlet and outlet temperature of the water, which mimics carotid blood flow. Preliminary studies have shown that the water temperatures measured by thermocouples are insensitive to the cross-sectional location of the thermocouple in the glass tube, as long as the thermocouple does not touch the glass surface. The design objective of the plate is to achieve a temperature reduction of at least 2.5°C along the tube ($T_{a,\mathrm{in}}-T_{a,\mathrm{out}}$) when the arterial blood flow rate is 240 ml/min [18]. All temperatures are recorded and data acquisition is performed using a LABVIEW® program running on a personal computer.

2.4 Experimental Protocol. The experimental setup is similar to a counter flow heat exchanger. We tested three cooling plate sizes (1 cm, 2 cm, and 3 cm in width) to study how to fix the cooling plate on the surface of the glass tube. The central line of the plate was in contact with the glass tube and the plate stays in its place primarily due to the pressing pressure from the two half gel blocks. For each plate, there were four trials representing different coolant temperatures (5°C, 10°C, 15°C, and 20°C). Experiments were repeated for three blood (water) flow rates (240 ml/min, 360 ml/min, and 480 ml/min). The experimental protocols are as follows:

1. The cooling plate was inserted into the gel blocks with tight physical contact with the glass tube using tapes wrapping around the outside of the gel. The gel phantom was then exposed to normal room temperature of approximately 25°C.
2. Initially, the warm water was pumped through the glass tube at a speed of 240 ml/min. The water temperature in the water bath was adjusted until the inlet temperature at the glass tube was approximately 37°C. The warm water was circulating continuously for 30 min to establish an initial steady state.
3. The coolant temperature in the circulator was set up at approximately 1°C, and the circular pump speed was adjusted until the coolant temperature inside the cooling plate was approximately 5°C. The cooling process was continued for approximately 15 min. Our preliminary experiments have shown that the cooling time was sufficiently long to achieve a steady state in the temperature decay along the glass tube.
4. Repeat step 3 for other coolant temperatures inside the coolant plate (10°C, 15°C, and 20°C).
5. Repeat steps 2–4 for other blood (water) flow rates through the glass tube (360 ml/min and 480 ml/min).

3 Results

We first tested how the cooling device was inflated once the coolant is circulated through the device. Device inflation can be addressed by lowering the pumping pressure, which results in a slow motion of the coolant circulating through the device. Because of the low flow rate of the coolant, temperature increases in the coolant due to heat gained from the environment to the coolant are significant. Therefore, one has to keep the coolant very cold in the circulator reservoir. Although the circulator used in the experiment has a refrigerator to lower the coolant temperature below 0°C, we prefer to set a lower limit of 1°C for the coolant. The pump speed was then adjusted to achieve a coolant temperature at the inlet of the cooling device to be as low as 5°C. Based on the pump power setting, all three cooling devices (1 cm, 2 cm, and 3 cm in width) were inflated. This created a problem for the 1 cm wide device. It was very difficult to ensure a closed surface contact between the device and the curved glass tube. It was later abandoned considering possible difficulty in future animal or clinical studies.

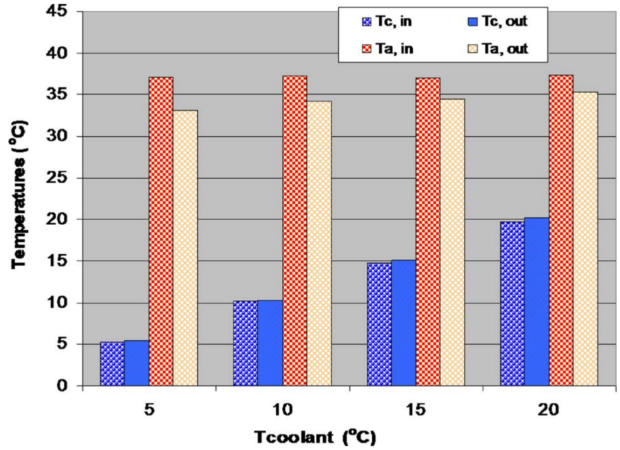

Fig. 4 Recorded temperature measurements at various measuring sites

A typical temperature variation during the cooling is illustrated in Fig. 4. The temperatures presented in the figure represent the steady state temperatures. Each group gives the measured $T_{c,\mathrm{in}}$, $T_{c,\mathrm{out}}$, $T_{a,\mathrm{in}}$, and $T_{a,\mathrm{out}}$. One notes that the coolant temperature only changes slightly from its inlet to its outlet with a variation of less than 0.5°C. It demonstrates that the surface temperature of the cooling device was relatively uniform during each cooling trial. The temperature of the warm water at the entrance of the glass tube was maintained relatively stable at approximately 37.20±0.15°C during the experiment. This is to ensure that the experimental condition mimics the actual physiological situation in the human neck.

Figure 5 compares the temperature reduction along the glass tube due to the cooling devices (2 cm and 3 cm in width). The flow rate of the water in the glass tube is 240 ml/min. The experimental data (symbols) are scattered; however, a linear line fitting the experimental data suggests that the 3 cm device is better than the 2 cm one in inducing more cooling to the water circulating in the glass tube. Overall, the 2 cm wide device results in 25% less cooling to the water circulating in the glass tube than the 3 cm wide device. In addition, the 3 cm wide device is much easier to handle in the experiment to ensure a good physical contact with

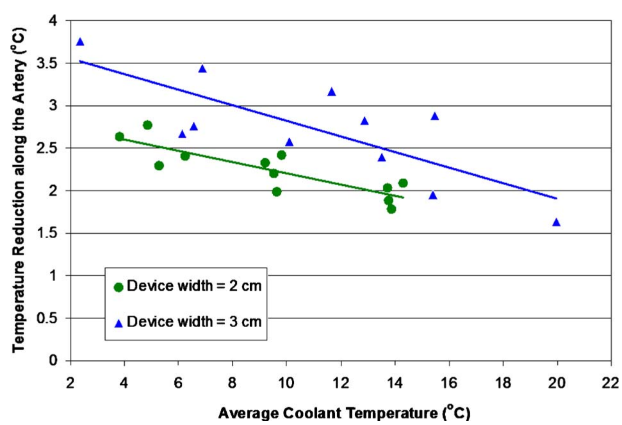

Fig. 5 Temperature reductions along the glass tube for the cooling devices of 2 cm and 3 cm in width. The flow rate is 240 ml/min.

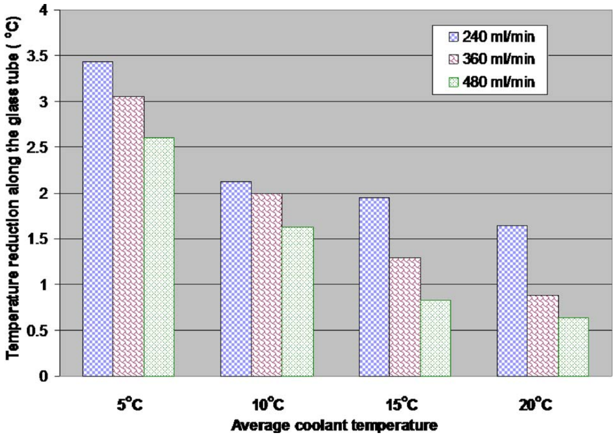

Fig. 6 The effect of the water flow rate in the glass tube on the temperature reduction along the tube

the glass tube surface. Both prototypes are capable of inducing more than 2.5°C temperature reduction in the water when its flow rate is 240 ml/min.

The reduction of the water temperature along the glass tube is influenced by the temperature of the coolant in the cooling device. Using the 3 cm wide cooling device, the temperature reduction is approximately 3.3°C when the coolant temperature is 5°C. Increasing the coolant temperature to approximately 20°C reduces the temperature reduction along the glass tube to almost 45% (1.8°C versus 3.3°C). The experimental results on the 3 cm wide prototype have shown that a temperature reduction of 2.5°C is still feasible when the coolant temperature is lower than 10°C and the water flow rate in the glass tube is 240 ml/min.

Blood flow rate in the common carotid artery in the human neck varies a lot ranging from the lower end of 240 ml/min to 480 ml/min. Its effect on the water temperature reduction along the glass tube is illustrated in Fig. 6. An increase in the water flow rate significantly attenuates the temperature reduction along the glass tube. This is expected since a high flow rate is associated with more thermal energy removal from the water for the same temperature reduction. Depending on the experimental setting, doubling the water flow rate lowers the temperature reduction, varying by 25–61%. For a patient with a higher blood flow rate in the common carotid artery, the cooling device should be designed longer to compensate the less temperature decrease associated with the higher blood flow rate.

4 Discussion and Conclusions

The previous theoretical analysis of the temperature decay along the common carotid artery has established the theoretical rationale of developing an interstitial cooling device to cool the common carotid arterial blood for open heart and neck surgery patients [18]. The result of the temperature reduction in the brain tissue in the theoretical study of 2.8°C (7 cm long) or 3.1°C (8 cm long) is much larger than the 1°C or 2°C required to be beneficial to those patients. The aim of the current experimental study is to test whether a prototype of the cooling device can actually result in the brain hypothermia illustrated in the theoretical study since the experimental condition may not completely duplicate the theoretical conditions. One of the issues encountered during the experiment is the physical contact between the cooling device and the glass tube mimicking the carotid artery. It has been assumed in the theoretical study that the contact is perfect. In our experiments, we rely on the pressure from the plastic container, which holds the gel blocks and tapes to ensure sufficient physical contacts between the cooling plate and glass tube. The slippery surfaces of the gel and glass tube also make it difficult to place the cooling plate in place, and adjustments are needed during the experiment. Thus, the scattered data observed in our experiment may be attributed to the uncertainty of the physical contact. The current design needs modifications to evaluate how to place and fasten the cooling device to the artery in future animal and clinical studies. For example, sutures or hooks may be necessary to address this issue. It is also important to keep in mind that the device should not interfere with the primary surgical procedures.

The emphasis of the study is on designing a prototype feasible to be used in future clinical applications rather than achieving an optimized design of the cooling device. To be consistent with the theoretical prediction, one design objective for the system is to reach a targeted temperature of 5°C at the outside surface of the flexible hollow cooling plate. We find that maintaining a coolant temperature at the reservoir of the circulator at 1°C is sufficient to deliver cold coolant (5°C) to the entrance of the cooling plate, using regular Teflon tubes (10 mm OD) wrapped with an insulation layer. Metal is a good thermal conductor for the cooling plate. However, in this study, we are more concerned about the easiness of manufacturing the hollowed plate using metal, physical damage to the tissue, leak-proof connection, and its biocompatibility. On the other hand, polyethylene sheets are tissue compatible and easy to be manufactured. We used a very thin sheet (<0.5 mm) to minimize thermal resistance to achieve the targeted device surface temperature. The experimental results have demonstrated the achievable goal of a cold coolant surface as low as 5°C at the entrance of the cooling device using water of 1°C in the reservoir of the circulator. From a practical point of view, in future animal or clinical studies, simply using an ice-water mixture in the reservoir without a refrigerator may help in size minimization of the system. Although polyethylene is not a good conductor, a very small coolant temperature difference between the inlet and outlet locations is found less than 0.5°C. It suggests an almost uniform temperature distribution on the surface of the cooling plate, and therefore, it is an acceptable material for the device. In future studies, traditional heat exchanger analyses can be used to further improve the design of the device while satisfying the constraints of the clinical applications.

One inherent limitation of the flexible cooling plate is the inflation of the device under the pumping pressure. It makes the placement of the plate and fixing it on the glass tube difficult. Because of this issue, we abandoned the designs of the 1 cm and 2 cm wide devices and prefer to use the 3 cm wide prototype. Our previous theoretical study has shown that the temperature reduction along the carotid artery is insensitive to the device width [18]. This seems to contradict our experimental observation where the 2 cm wide device resulted in a cooling along the glass tube 25% smaller than by using the 3 cm wide prototype. One possibility may be the less physical contact associated with the narrower cooling device. Another deviation from the theoretical prediction is due to the flexible cooling plate that can provide a bigger contact surface area with the glass tube. In the theoretical simulation, the device is modeled as a flat surface; therefore, direct contact with the artery is limited to a straight line along the artery. On the other hand, in the experiment, the cooling plate may be bent to maximize the contact area with the glass tube. This may be the reason why a slightly larger temperature decay of 3.3°C in the experiment is observed than in the simulation (3.1°C) (see Fig. 6 in Wang and Zhu [18]) when the device is 8 cm long and the surface temperature is kept at 5°C. Nevertheless, the challenge faced in future clinical and animal studies is still how to maximize the contact area without interfering with the primary surgical procedures.

Despite the scattering of data, the experimental results have established clear trends of its dependence on both the coolant temperature and water flow rate in the glass tube. In principal, the temperature decay along a glass tube is approximately proportional to the driving force, i.e., temperature variation in the setup. In this study, the maximal temperature variation is between the water temperature at the entrance of the glass tube and the temperature of the coolant. Therefore, the temperature variation is 32°C (37−5°C) when the coolant temperature is 5°C while it is 17°C when the coolant temperature is 20°C. One would expect to see an almost 50% decrease in the temperature reduction along the glass tube. Our measurement of 45% decrease in the temperature reduction from the coolant of 5–20°C agrees well with the theoretical prediction.

Our results have illustrated a decrease in the temperature reduction with an increase in water flow rate in the glass tube. Previous theoretical analyses have demonstrated a reciprocal relationship between the blood flow rate and temperature decay along a blood vessel [18,23]. This relationship is highly approximate since the heat transfer between a blood vessel and its surrounding tissue is primarily determined by the lateral conduction resistance in the cross-sectional plane. The energy transferred in the cross-sectional plane should be reflected by the product of the temperature decay along the vessel ΔT and the blood flow rate Q, i.e., $\rho CQ\Delta T$, where ρ is blood density and C is specific heat. Therefore, if the total heat transfer rate in the lateral direction is almost unchanged, the total temperature decay along the vessel is almost inversely proportional to the blood flow rate. For example, if blood flow rate is doubled, temperature decay should be halved. Our experimental results have shown a decrease ranging from 25% (T_c =5°C) to 61% (T_c=20°C) in the water temperature reduction in the glass tube when the water flow rate is increased from 240 ml/min to 480 ml/min. Although not completely the same as the theoretical prediction, the reciprocal trend of a less temperature reduction with a larger water flow rate is similar to the theoretical analyses.

In conclusion, the current experimental study has identified a cooling prototype design, which is capable of inducing sufficient temperature reduction along the common carotid artery in the human neck. Water at 5°C can be delivered at the device entrance when using above 0°C water in the reservoir. The surface temperature of the device is almost uniform. Despite its limitations, the experimental results agree generally well with the theoretical predictions. The 8 cm long and 3 cm wide device with a coolant temperature lower than 10°C is capable of inducing a temperature reduction of at least 2.5°C along the glass tube filled with water circulating at 240 ml/min. For higher water flow rates, one needs to increase the length of the device and/or lower the coolant temperature to achieve a similar temperature decay along the glass tube.

Acknowledgment

This work was supported in part by a grant from Pennsylvania Keystone Innovation Zone (KIZ) Grant and a grant from the State of Maryland TEDCO fund.

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