

INFECTION RATES IN A TRAUMATIC BRAIN INJURY COHORT TREATED WITH  
INTRAVASCULAR COOLING CATHETERS

by

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## INFECTION RATES IN A TRAUMATIC BRAIN INJURY COHORT TREATED WITH INTRAVASCULAR COOLING CATHETERS

Donald T. Schleicher II, M.S.

University of Pittsburgh, 2008

Each year, in the United States, 235,000 individuals sustain a traumatic brain injury requiring hospitalization. Patient outcome from severe traumatic brain injury is improved with intensive care management of pathophysiological processes developing in the days following the injury. An important secondary complication of traumatic brain injury is fever, which is known to worsen neurologic outcome. Our institution has recently developed an approach to combat fever through the prophylactic use of intravascular cooling catheters, a treatment termed controlled normothermia.

We have recently demonstrated that controlled normothermia reduces both core and brain temperature and can improve the intracranial milieu that may facilitate recovery. A major drawback to the systematic use of controlled normothermia is an increased risk of infection, or delayed diagnosis of infection by masking of fevers. In the current study, we evaluated whether “controlled normothermia”, the prophylactic use of intravascular cooling catheters in severe traumatic brain injury, is associated with increased infection rates during the intensive care stay.

Utilizing a matched cohort study and data from the Brain Trauma Research Center’s database, a retrospective study was performed. The data was taken from the Brain Trauma Research Center’s traumatic brain injury registry, and was matched on age, gender, and Glasgow Coma Score. After analysis, the results of the study indicated fewer infections in the controlled

normothermia group; the rates of bloodstream infections were statistically lower in the controlled normothermia group.

The current study demonstrates that prophylactic use of intravascular cooling catheters in severe traumatic brain injury is not associated with an increased risk of infection. The public health significance is that these results lend further support to the concept of controlled normothermia as a treatment for severe traumatic brain injury. Further study may prove that controlled normothermia is effective in improving neurologic outcomes from traumatic brain injury, which remain the leading cause of death under age 45 in the United States.

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## **PREFACE**

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## 1.0 INTRODUCTION

Traumatic brain injury is a major public health concern in the United States. Each year around 1.5 million people sustain a traumatic brain injury. The main mechanisms by which traumatic brain injuries occur are through motor vehicle accidents, falls, assaults, motor vehicle versus pedestrians, and recreational vehicle accidents. Each year, of these 1.5 million around 50,000 people die, either in the hospital or at the scene of the injury, while another 235,000 are hospitalized.

The goal of modern intensive care management of severe traumatic brain injury is to minimize secondary complications that may worsen the injury in the days to weeks following the traumatic insult. For example, ischemia following a traumatic brain injury can lead to brain tissue receiving inadequate oxygen, further complicating the injury.

An important secondary complication of traumatic brain injury is fever. Fever following a severe traumatic brain injury can result from multiple etiologies including infection, disturbances in the body's thermo-regulation, or because of drugs administered to patients in the intensive care unit.

Fever control following traumatic brain injuries have long proved difficult. Historical approaches to fever management following traumatic brain injury have produced only moderate results at best. In our institution, a novel approach has been recently adopted in that intravascular cooling catheters are placed prophylactically upon admission in an effort to avoid

fever and its negative consequences for the already injured brain. When cooling catheters are placed prophylactically, this treatment approach is termed controlled normothermia. Preliminary results indicate that controlled normothermia produces tangible benefits for the patient in the form of reduced secondary brain injury and improved temperature control.

The purpose of the current study is to evaluate whether the therapeutic approach of controlled normothermia is associated with increased rates of nosocomial infections.

## 2.0 RELEVANT LITERATURE REVIEW

Fever following severe traumatic brain injury occurs frequently in the injured patient, and has been associated with worsened neurological outcomes. Fever occurs in up to 70% of patients following severe traumatic brain injury.<sup>2</sup> Febrile episodes in the recovering patient can occur in multiples and can be of extended duration throughout the patients' stay in the neurological intensive care unit.

Fever in the neurological intensive care unit is also correlated with length of stay in the hospital. Kilpatrick et al<sup>18</sup> reported that 15% of patients in the neurological intensive care unit for less than 24 hours suffer from a febrile episode while 93% of patients who remain in the intensive care unit for more than 7 days have a febrile episode. Early hyperthermia (within 48 hours post injury) is associated with poor outcomes,<sup>11</sup> while fever in pediatric traumatic brain injury is associated with both longer length of stay in the hospital and poor neurologic outcome.

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Hyperthermia following severe traumatic brain injury may result from both infections and non-infectious causes. Disruption of the hypothalamic set point due to traumatic brain injury or intracranial pathologies such as sub-arachnoid hemorrhage or intraparenchymal hemorrhage may also induce fever. Fever may alternatively occur in response to medications or transfusions or from atelectasis after surgery, whether surgery is related to the traumatic brain injury or not.

Treatment of fever has been correlated with improved outcomes in multiple neurological insults. In the setting of severe traumatic brain injury, fever control has a sound theoretical basis for improving outcomes, but this has not yet been demonstrated with a prospective clinical trial.<sup>1</sup>

In the late 1990's, our institution adopted an aggressive fever management protocol for all patients in the neurological intensive care unit with rectal temperatures greater than 38°C. This protocol, involving standing anti-pyretic medications, surface cooling, and gastric ice lavage, led to a significant reduction in febrile episodes, but 47% of the patients in the intensive care unit continue to develop febrile episodes.<sup>18</sup>

In the search for improved fever control, our institution participated in a multi-centre trial investigating the utility of an intravascular cooling catheter to treat fever in the neurological intensive care unit. A prospective, randomized controlled trial was performed comparing standard fever management (acetaminophen and an external cooling blanket) with intravascular cooling catheters. The intravascular cooling catheter group experienced a 64% reduction in fever burden, determined by the time spent febrile (degree hours). Treatment groups were equivalent in rates of infection and use of antibiotics.<sup>10</sup> The study concluded that intravascular cooling catheters were superior to conventional means of fever control with risks equivalent to that of a central line catheter placement.

Our institution then began an evaluation of a treatment approach termed controlled normothermia. Controlled normothermia is the prophylactic placement of an intravascular cooling catheter at admission to the neurologic intensive care unit in an effort to prevent the fever from occurring in the first place, thus reducing or eliminating its detrimental effects. Controlled normothermia has been shown to lower intracranial pressure, lower intracranial fever burden, and increase brain tissue oxygenation in severe traumatic brain injury.<sup>23</sup>

A major concern in controlled normothermia is that patients will suffer increased rates of nosocomial infections. The current study examines whether controlled normothermia, the prophylactic use of intravascular cooling catheters, is associated with increased rates of infections in severe traumatic brain injury patients in the neurologic intensive care unit.

### **3.0 STUDY DESIGN AND METHODOLOGY**

The design of this study is a matched cohort study. A cohort of patients, those with a severe traumatic brain injury was examined in two separate groups: patients who received an intravascular cooling catheter and patients who had not. The intravascular cooling patients were selected as the “exposed group” in this study and were matched on age, gender, and severity of injury via the Glasgow Coma Score with patients who did not receive the intravascular catheter treatment. The two groups were then examined closer to see what infections they contracted and at what times. The infection rates for these two groups were then compared in order to determine whether having an intravascular cooling catheter placed leads to a higher incidence of infection, specifically bloodstream, respiratory, urinary, cerebral spinal fluid, and deep wound infections.

All patients examined in this article were under an Institutional Review Board approved treatment regimen and data collection protocol. This approval was through the University of Pittsburgh Brain Trauma Research Center.

The patient cohort under study, those with severe traumatic brain injuries, had information previously collected and compiled into a larger database. The Brain Trauma Research Database contains over 750 patients who sustained a severe head injury. Along with the demographic data, a vast quantity of medical data is collected from these patients. In order to

collect this type of data, the patient was informed of the study and granted collection and use of this data to the Brain Trauma Research Center. A copy of the Internal Review Board approved consent form is filed under appendix A. In addition to the consent form, a preliminary data collection form is also included under appendix A.

Forty eight patients were identified who had received intravascular cooling catheters. The patients were then matched with corresponding controls based on the patients' age, gender, and severity of injury via the admitting Glasgow Coma Score. These three factors (age, gender, and injury severity) were chosen, because it has been well documented that these three variables have a large impact on the outcome of the patient. Clinical experience has shown that younger patients often have better outcomes when faced with a traumatic brain injury than older patients.<sup>24</sup> It is documented that men often times have better outcomes than females.<sup>24</sup> Injury severity measured by GCS, has been widely documented to affect outcomes specifically: the worse a patient is initially the lower the GCS and thus the worse the outcome; better GCS scores mean less severe injuries and often times, barring complications, better outcomes.

Once the age, gender, and injury severity data were obtained for the catheter group, another Access search located patients that had similar age, gender and injury severity who did not receive the cooling catheters. By matching exactly on gender,  $\pm 2$  years for age, and  $\pm 1$  Glasgow Point for GCS, these three factors were adequately controlled for in this study. Between the two groups, the total number of patients in this study was 96 (48 who received cooling catheters and 48 matched on age, gender, and injury severity who did not receive catheters). Three patients and their corresponding controls were removed from the study because the exposed patients died within 14 days of admission.

After selection of “exposed” and “control” groups, all of the patients’ demographic data were entered into a large Excel spreadsheet. The data that were included in this initial spreadsheet were age, injury severity, gender, date of injury, date of hospital admission, death date, 14 days post admission, date of catheter insertion, and the date of catheter removal, and whether or not the patient had an invasive surgery or a skull fracture. Once these data were obtained, further searches revealed bacterial culture data and other cultures, such as fungal infections.

Another complication that arose from the data is that the catheter insertion time was different from the admission time on six of the intravascular patients. This posed a problem because it was unknown as to whether the catheter was placed because a fever was beginning to develop. Either way, the catheter was not inserted prophylactically and thus these six patients and their corresponding controls were removed from analysis. After the removal for death and non-prophylactic use, the total population under study is 78 with 39 being patients who received an intravascular cooling catheter on admission and 39 who did not, matched on age, gender, and injury severity.

Upon completion of the data collection, Statistical Analysis Software (SAS) performed the statistical calculations. Specifically, the patient characteristics for both the exposed and unexposed groups were examined through chi-square analysis for proportions and with Wilcoxon Tests for comparison of the means. Infection outcomes between the two study groups were measured with both the chi-square test where applicable, or the Fischer Exact test when appropriate.



## 4.0 RESULTS

The patient population that comprised the cohort under study is summarized in the chart below.

Figure 1 shows the general overview for the demographics of population under study.

**Table 1: Clinical Cohort Characteristics and Culture Results**

Cohort Characteristics	Intravascular Cooling Catheters n=39	Non-Intravascular Cooling Catheters n=39	Relative Risk	95% Confidence Interval
Gender (Male)	33	33	*	p-value .78
Mean Age (Years)	35.9	35.7	*	p-value .85
Mean GCS	5.9	5.8	*	p-value .65
Invasive Operations	74.4%	76.9%	*	p-value .79
Skull Fracture	53.8%	30.8%	*	p-value .039
Deep Wound Infections	2.6%	5.1%	.51	.05-5.4
Bronchial Alveolar Lavage	84.6%	71.8%	1.18	.93-1.5 *
Blood Culture Isolate	35.9%	59%	0.61	.37-.99 *
Clostridium Difficile Toxin	5.1%	2.6%	2	.19-21.2
Cerebral Spinal Fluid Isolate	10.3%	10.3%	1	.27-3.7
Nasal Swab Isolates	2.6%	2.6%	1	.06-15.4
Vancomycin Resistant Enterococcus	2.6%	2.6%	1	.06-15.4
Sputum Culture Isolate	28.2%	43.60%	0.65	.35-1.2 *
Catheter Tip Isolate	5.1%	0%	Undefined	Undefined
Urine Culture Isolate	15.4%	15.4%	1	.35-2.8

\* Denotes borderline significance

The first step to examining the results was to examine the matching of the two groups to confirm that the matching protocol was adequate for the study population. The main determinant to show that age had been adequately controlled for was the mean ages between the two groups. The intravascular catheter group had a mean age of 35.9 years while the control group had a mean age of 35.7 years. These two means for the groups were not statistically different. In addition to the t-test, a Wilcoxon two sample test was used. The p-value for this tested showed no statistical difference between the two groups. Again, the mean GCS for the two groups were examined with the results being 5.9 and 5.8 for the catheter group and the control group respectively. In addition to the t-test, a Wilcoxon two sample test was performed on the data. The GCS between the two groups proved to be not statistically significant. Finally, the gender confounder was examined. While female gender was less prevalent than male gender in the two groups, the proportion of females in each group is the same (six in each group).

Once the data were shown to be properly matched, the task of finding statistically significant results began. Two of the more common confounding factors skull fractures and surgical operations were examined. There was a statistically significant difference in skull fractures between the catheter group and the control group (p-value .039; 54% vs. 31%), such that the catheter group had more skull fractures than the control group. Since this was a clinically relevant and statistically significant confounder, it was adjusted for in the analysis. The second potential confounder, the invasive surgical operations, was examined; by both 2x2 tables and by statistical test, no difference was noted between the two groups. Since invasive surgical operations were not a statistically significant difference between the two groups, an invasive surgical procedure is not a strong confounder. Tables 2 through 4 show final data for the outcomes where p-values were less than .20.

**Table 2: Association between Cooling Catheters and Bronchial Alveolar Lavage Results for All**

**Patients**

	Infection Present	Infection Absent
Exposed(normothermia)	33	6
Control	28	11

RR=1.18

p-Value= .22

**Table 2 continued: Patients with Skull Fracture**

	Respiratory Infection Present	Respiratory Infection Absent
Exposed (normothermia)	18	3
Control	9	3

RR=1.14

**Table 2 continued: Patients without Skull Fracture**

	Respiratory Infection Present	Respiratory Infection Absent
Exposed (normothermia)	15	3
Control	19	8

RR=1.18

**Table 3: Association between Cooling Catheters and Blood Culture Results for All Patients**

	Blood Infection Present	Blood Infection Absent
Exposed (normothermia)	14	25
Control	23	16

RR=.61

p-Value=.03

**Table 3 continued: Patients with Skull Fracture**

	Blood Infection Present	Blood Infection Absent
Exposed (normothermia)	8	13
Control	8	4

RR=.57

**Table 3 continued: Patients without Skull Fracture**

	Blood Infection Present	Blood Infection Absent
Exposed (normothermia)	6	12
Control	15	12

RR=.60

**Table 4: Association between Cooling Catheters and Sputum Culture Results for All Patients**

	Respiratory Infection Present	Respiratory Infection Absent
Exposed (normothermia)	11	28
Control	17	22

RR=.65

p-Value=.26

**Table 4 continued: Patients with Skull Fracture**

	Respiratory Infection Present	Respiratory Infection Absent
Exposed (normothermia)	3	18
Control	6	6

RR=.29

**Table 4 continued: Patients without Skull Fracture**

	Respiratory Infection Present	Respiratory Infection Absent
Exposed (normothermia)	8	10
Control	11	16

RR=1.09

By utilizing two by two tables, the relative risks for each of the three types of cultures are calculated. Utilizing the relative risk allows this paper to justify the risk associated with cooling catheter insertion. Being that skull fracture was a confounding variable, analyses were stratified by this factor. There are no statistically significant differences between the exposure group and the unexposed group (p-value  $>.2$ ) with regard to deep wound infections, clostridium difficile isolates, cerebral spinal fluid isolates, methicillin resistant staphylococcus aureus, vancomycin resistant enterococcus, catheter tip isolates (either the cooling catheter for the catheter group or a central line catheter for the non cooling catheter group), and urine culture isolates.

## **5.0 DISCUSSION**

The present study demonstrates that controlled normothermia, the prophylactic use of intravascular cooling catheters to prevent fever, does not increase overall infection rates in patients after a severe traumatic brain injury insult. Furthermore, controlled normothermia is associated with a significant decrease in the rates of systemic bacteremia. Controlled normothermia is an effective means of avoiding and treating fever in severe traumatic brain injury without an increase in infection rates.

### **5.1 INTENSIVE CARE TREATMENT FOR TRAUMATIC BRAIN INJURY**

The goal of intensive care management in the neurologic intensive care unit is to assist the patient in achieving the best neurologic and physical outcome. The goals of effective intensive care management include monitoring and treating potential complications that can arise throughout the patients' stay in the hospital. Some of the complications that can arise are increased intracranial pressure, decreased cerebral perfusion, electrolyte imbalance, infections, and hyperthermia.

To combat the negative effects of hyperthermia, the intensive care unit utilizes different methods. Some of the methods include anti-pyretic medications, cooling blankets, and gastric ice lavage. Currently, the neurological intensive care unit in our institution utilizes an aggressive

prophylactic catheter-based cooling technique to control the patient temperature. This treatment approach of controlled normothermia, the use of intravascular cooling catheters, is a safe and effective means of combating hyperthermia.

This new approach, controlled normothermia, is an effective, novel, and innovative approach to fever management in the intensive care unit. The current study examined whether controlled normothermia is associated with increased rates of infection in severe traumatic brain injury. The results of the study lend support to the use of controlled normothermia as a fever control technique upon admission to the neurologic intensive care unit.

## **5.2 INFECTIONS AFTER A SEVERE TRAUMATIC BRAIN INJURY**

Patients suffering from severe traumatic brain injury are at a risk for nosocomial infections including respiratory, blood, cerebral spinal fluid, urinary tract, catheter, and wound infections.

There was no statistically significant findings between the two treatment groups in the majority of the culture tests; specifically, the deep wound cultures, the drug resistant strains of VRE and MRSA cultures, clostridium difficile toxin screens, the cerebral spinal fluid cultures, the urinary cultures and the catheter tip cultures.

The first objective of this study examined specifically the incidence of infection between the treatment and the control groups. Since many of the cultures were not statistically different between the two treatment arms, it can be concluded that the infections rates for these cultures did not differ between the two treatment groups. After analysis, the three cultures that had p-values lower than .20 were the sputum, the bronchial alveolar lavage, and the blood culture.



The sputum and the bronchial alveolar lavage cultures are respiratory-based cultures and are associated strongly with the length of time a patient stays on the ventilator.<sup>5</sup> These respiratory infections often do not indicate a systemic infection, but a ventilator-associated infection.<sup>5</sup> It can be concluded that these two cultures do not offer significant information as to the rates of systemic infection between the two treatment arms.

The blood culture data suggest a statistically significant difference between the two treatment groups. The controlled normothermia group had statistically fewer infections when compared to the control group. This observation lends credence to the idea of prophylactic treatment with intravascular cooling catheters.

The second objective of this study was to examine whether the catheter itself causes an increase in infections in the severe traumatic brain injured patient. By examining the catheter tip culture data, it can be seen that, between the two groups, there is no statistically significant difference between the controlled normothermia arm and the control arm. In previous articles, it was theorized that the blood circulating around the cooling catheter would often stagnate around the catheter and provide a media for bacterial growth.<sup>10</sup> In addition to the blood stagnation around the catheter, the increased lumen size for the intravascular cooling catheter and the resulting increased incision could lead to increased infection rates. The data obtained in this study indicate the catheter causes neither a statistically significant increase in the catheter tip based infections nor the systemic blood stream infections.

Prophylactic treatment with intravascular cooling catheters has multiple advantages when used in a severe traumatic brain injury patient. First, the catheters provide optimum environment for brain healing by keeping the patient at normothermic levels. Secondly, the data show that

there is not an increased risk for catheter-based infections. Finally, the rates of systemic blood borne infections appear to decrease in the patients treated with intravascular cooling catheters.

### **5.3 STUDY LIMITATIONS**

A matched cohort study to examine the effects of intravascular cooling catheters on infection rates is an effective method of analysis. However, as with all studies, this study has limitations including small sample size and a retrospective design.

In addition to the sample size, the study design was retrospective in nature. It was comprised of chart reviews and previously reported data. This notion can raise a question as to the completeness of the data. The chart reviews were based off billing information. The billing records indicate how many cultures each patient received and even included billing costs for the length of time that the intravascular cooling catheter was inserted.

The final limitation was in the catheter group itself. When on the intensive care unit, the white blood cell count is monitored, along with the fever. If the patient is unable to develop a fever, the infection may be missed by the nursing staff. This could lead to a lower number of cultures in the normothermia group. This can bias the data by showing an artificial decrease in the number of infection in the catheter group.

## **6.0 CONCLUSIONS**

The current study demonstrates that controlled normothermia, the prophylactic use of intravascular cooling catheters in severe traumatic brain injury, is not associated with an increased risk of infection either from the catheter itself or from the inability to develop a fever. Controlled normothermia was associated with a significant decrease in the rates of positive blood cultures. These results lend further support to the concept of controlled normothermia as a valid treatment for severe traumatic brain injury. With this prophylactic treatment, patients can benefit from controlled normothermia to provide a better environment conducive to brain healing, without the theoretical increased infection risk.

**APPENDIX: INFORMED CONSENT FORMS AND SCREENING SHEET**



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## CONSENT TO ACT AS A SUBJECT IN A CLINICAL STUDY

**TITLE: Biochemical analysis of cerebrospinal fluid and brain tissue following severe head injury**

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SOURCE OF SUPPORT: National Institute of Health

**DESCRIPTION:** \_\_\_\_\_ is being asked to participate in this clinical research project because he/she has sustained a severe head injury. The purpose of this

study is to examine the biochemical secondary mediators (chemical components in the brain) that occur after brain injury. Markers of ischemia (low blood flow) and cell death are to be examined and compared with his/her physiologic values (heart rate, blood pressure, blood flow, oxygenation values, etc that are displayed on the patient's monitor) during the course of five days after hospitalization. It is of research interest to compare physical and psychological outcome (physical and mental recovery and abilities) after traumatic brain injury with markers of ischemia. Our goal of this research is to further understand the relationship of ischemia and outcomes in order to improve these neurological outcomes in the future. In the next five years we anticipate entering 300 patients into the study. Male and females are to be included within the age range of 16-75 years old.

If you agree to your relative's participation in this study, you have consented to the following research that is not part of your relative's routine medical care:

1. Release of cerebrospinal fluid (the fluid responsible for brain swelling) to be examined for biochemicals. Approximately 6 tablespoons per day for 5 days or as long as the catheter is required for routine care will be collected. This fluid is normally discarded and no additional fluid will be drawn. Drainage of the cerebral spinal fluid is a technique we normally use to control brain swelling, and the catheter is required to monitor brain swelling as routine care.
2. Physiological data (heart rate, blood pressure, blood flow, global and local oxygenation values, etc) that is displayed on the patient monitor will be collected and stored in a computer database to compare with the chemical values and blood flow values for five days from admission. The data will be stored in an anonymous form with each patient being assigned a number to maintain confidentiality. Information from the chart (labwork, medications, etc) will also be recorded in this database as well as outcome information at 3, 6, 12 and 24-month follow-up visits. All data is coded with a unique identifying number to maintain confidentiality.
3. Release of a blood sample twice a day to be examined for biochemicals and compared to those within the cerebrospinal fluid. Approximately 4 tablespoons per day for 5 days or as long as the catheter is required for routine care will be collected. Samples will be taken from a tube (indwelling catheter) that is placed as a routine standard of care. All efforts will be made to obtain a sample when other routine laboratory tests are taken.

If your relative requires surgery for removal of damaged brain tissue or blood clots in the brain, we also ask permission for:

4. Release of a small amount of tissue that was removed during surgery (approximately 1/2 inch) to be examined for chemicals associated with brain injury. Only damaged tissue that is removed as part of the surgery will be examined. This tissue is normally discarded. No additional tissue is removed for this research study.

If you agree to the participation of your relative in this research project, use of their biological sample will be under the control of the primary investigator. The above donated fluid and tissue may be released to other investigators to study various components of brain injury. All data is coded with a unique identifying number to maintain confidentiality. The samples will be stored for at least 5 years. You do not have to agree to the release of samples in order for your relative to participate in the other

portions of this study. The results of this study are valid for research purposes only and will not be provided to you.

**RISKS AND BENEFITS:**

There is no direct benefit to the patient from this study; however, analysis of cerebrospinal fluid may lead to improved means for treatment in future head injured patients. All patients eligible for this study have a cerebrospinal drain placed for clinical need. This catheter has a risk for infection. This risk is not increased by the collection of these samples. Blood sampling is obtained by an indwelling tube (catheter) that is standard of care. All efforts will be made to collect this sample to coincide with routine daily blood tests. A rare risk is infection of this catheter from sampling (occurs in < 1% or < 1 out of 100 patients).

An additional risk of this research is a breach of confidentiality. All patients are coded with a unique identifying number as they enter the study, and all subsequent samples and outcome information are coded with the same number. All efforts will be taken to maintain the anonymity of this valuable information.

**NEW INFORMATION:**

If new information, either good or bad, about chemical components responsible for brain swelling comes to the attention of the investigator during the course of this study and which may relate to your willingness to continue with his/her participation, it will be provided to you.

**COST AND PAYMENTS:**

There is no charge for participating in this research study. Research chemical analysis is the responsibility of the investigator. There will be no payments made for participation in this study. All other exams are routine medical care, will be billed in the standard fashion and become the responsibility of the patient. Your relative's biological sample may lead, in the future, to new inventions or products. If the research investigators are able to develop new products from the use of your relative's biological sample, neither you nor your relative will receive any money for the donation of this biological sample.

**CONFIDENTIALITY:**

Any information about your relative from this research will be kept as confidential (private) as possible. Your relative's identity on these records will be indicated by a case number rather than by their name, and the information linking these case numbers with their identity will be kept separate from the research records. Only the researchers listed on the first page of this form and their staff will have access to your relative's research records, and are responsible in making them anonymous for the other research investigators. You will not be identified by name in any publication of research results unless you sign a separate form giving your permission (release).

This research study will involve the recording of current and/or future identifiable medical information from your relative's hospital and/or other healthcare provider (e.g. physician office) records. The information that will be recorded will be limited to information concerning physiological data obtained in the intensive care unit, injury related information and neurological outcome information. This information will be used for the purpose of relating factors involved in the patient's care that may affect

overall outcome. This research will not involve the generation of information that will be placed within the patient's medical record. All information obtained will be research purposes only, and therefore uninterpretable for clinical reasons.

In addition to the investigators listed on the front page of this authorization (consent) form and their research staff, the following individuals will or may have access to identifiable information (which may include your relative's identifiable medical record information) related to your relative's participation in this research study: Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office, as well as representatives of the National Institutes of Health may review your relative's identifiable research information (which may include your relative's identifiable medical record information) for the purpose of monitoring the appropriate conduct of this research study. While the study sponsor understands the importance of maintaining the confidentiality of your relative's identifiable research and medical record information, the University of Pittsburgh Medical Center and the University of Pittsburgh cannot guarantee the confidentiality of this information after it has been obtained by the study sponsor. In unusual cases, the investigators may be required to release identifiable information (which may include your relative's identifiable medical record information) related to your relative's participation in this research study in response to an order from a court of law. If the investigators learn that your relative or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.

Any tissue or fluid samples that are given to other investigators will be stripped of any identifying information. All research records will be securely filed for at least five years according to the University of Pittsburgh policy.

**RIGHT TO WITHDRAW:**

Your relative's participation in this research study, to include the use and disclosure of his/her identifiable information for the purposes described above, is completely voluntary. (Note, however, that if you do not provide your consent for the use and disclosure of your relative's identifiable information for the purposes described above, he/she will not be allowed, in general, to participate in the research study.) Whether or not you provide your consent for participation in this research study will have no affect on your relative's current or future relationship with the University of Pittsburgh. Whether or not you provide your consent for participation in this research study will have no affect on your relative's current or future medical care at a University of Pittsburgh Medical Center hospital or affiliated health care provider or your relative's current or future relationship with a health care insurance provider.

Your relative's doctor is involved as an investigator in this research study. As both your relative's doctor and a research investigator, s/he is interested both in your medical care and the conduct of this research study. Before agreeing to participate in this research study, or at any time during your relative's study participation, you may discuss your relative's care with another doctor who is not associated with this research study. You are not under any obligation to participate your relative in any research study offered by the doctor. You may withdraw, at any time, your consent for participation in this research study, to include the use and disclosure of your relative's identifiable information for the purposes described above. (Note, however, that if you withdraw your consent for the use and disclosure of your relative's identifiable information for the purposes described above, your relative will also be



withdrawn, in general, from further participation in this research study.) Any identifiable research or medical record information recorded for, or resulting from, your relative's participation in this research study prior to the date that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above. If you withdraw your relative, or your relative refuses to continue to participate, samples will continue to be stored with destruction of the linkage code to your relative's identity.

To formally withdraw your consent for participation in this research study you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form.

Your decision to withdraw your consent for your relative's participation in this research study will have no affect on your relative's current or future relationship with the University of Pittsburgh. Your decision to withdraw your consent for participation in this research study will have no affect on your relative's current or future medical care at a University of Pittsburgh Medical Center hospital or affiliated health care provider or your relative's current or future relationship with a health care insurance provider.

**COMPENSATION FOR INJURY:**

University of Pittsburgh researchers and their associates who provide services at the University of Pittsburgh Medical Center recognize the importance of your voluntary participation in their research studies. These individuals and their staffs will make reasonable efforts to minimize, control, and treat any injuries that may arise as a result of this research. If you believe that your relative is injured as a result of the research procedures being performed, please contact immediately the Principal Investigator or a co-investigator listed on the first page of this form.

Emergency medical treatment for injuries solely and directly related to your relative's participation in this research study will be provided to your relative by the hospitals of the University of Pittsburgh Medical Center. It is possible that the University of Pittsburgh Medical Center may bill your insurance provider for the costs of this emergency treatment, but none of these costs will be charged directly to your relative. If research-related injury requires medical care beyond this emergency treatment, your relative will be responsible for the costs of this follow-up care unless otherwise specifically stated below. You will not receive any monetary payment for, or associated with, any injury that your relative may suffer in relation to this research.

**VOLUNTARY CONSENT:**

If your relative regains the ability to provide informed consent, the study will be explained to them and they will be asked to decide on their further participation.

The above information has been explained to me and all of my questions have been answered. Any further questions I have about this research study will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions be answered by the listed investigator. Any questions I have about my rights as a research subject will be answered by the Human Subject

Protection Advocate of the IRB Office, University of Pittsburgh 1-866-212-2668. By signing this form, I agree to allow participation of my relative in this research study. A copy of this consent form will be given to me.

\*\*\*\*\*

I give permission for my relative's biological samples/data to be used, without personal identifiers, in other research projects involving the study of brain injury.

YES \_\_\_\_\_ NO \_\_\_\_\_

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**Participant's Name (print)**

The above-named individual is unable to provide direct consent for study participation because he/she has suffered a severe traumatic head injury, rendering the individual comatose (unconscious).

Therefore, by signing this form, I give my consent for his/her participation in this research study.

\_\_\_\_\_  
**Representative's Name (print)**

\_\_\_\_\_  
**Relationship to Participant**

\_\_\_\_\_  
**Representative's Signature**

\_\_\_\_\_  
**Date**

**CERTIFICATION OF INFORMED CONSENT:**

I certify that I have explained the nature and purpose of this research study to the above-named individual(s) and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions as they arise.

\_\_\_\_\_  
**Printed Name of Person Obtaining Consent**

\_\_\_\_\_  
**Role in Research Study**

\_\_\_\_\_  
**Signature of Person Obtaining Consent**

\_\_\_\_\_  
**Date**

**CONTINUED PARTICIPATION CONSENT:**

I have been informed that I am currently participating in a research study. I have read (or have had read to me) and understand this consent form which was previously signed by my legal representative. Any questions I have pertaining to the research have been and will continue to be answered by the investigators listed in the beginning of this consent form at the telephone numbers given. My signature below means that I freely agree to continue to participate in this research study.

By signing below, I agree to continue my participation in this research study. A copy of this consent form will be given to me.

\_\_\_\_\_  
**Date**

\_\_\_\_\_  
**Participant's Signature**

## Brain Trauma Research Center CHECK LIST

DATE:

PHYSICIAN:

NURSE:

<b>UID:</b>	<b>Bed:</b>	<b>Study:</b> <input type="checkbox"/> Control <input type="checkbox"/> Hypothermia <input type="checkbox"/> Not Randomized <input type="checkbox"/> N/A <input type="checkbox"/> Pilot Subject	<b>SS #:</b>	<b>Name:</b>	
<b>Injury Date/Time:</b>		<b>Data:</b> <input type="checkbox"/> Real Time <input type="checkbox"/> Bowman CBF Monitoring <input type="checkbox"/> Micro Monitoring <input type="checkbox"/> Brain O <sub>2</sub> Monitoring <input type="checkbox"/> Tissue <input type="checkbox"/> BIS <input type="checkbox"/> Somanetics <input type="checkbox"/> Alsius	<b>MR #:</b>		
<b>Arrival Date/Time:</b>			<b>Date of Birth:</b>		
<b>Unit Arrival Date/Time:</b>		<b>Consent:</b> Next of Kin Name/Date/Time:  _____	<b>Date Accuracy:</b> <input type="checkbox"/> Correct <input type="checkbox"/> Day Estimated	<b>Function of Injured:</b> <input type="checkbox"/> Driver <input type="checkbox"/> Occupant(front) <input type="checkbox"/> Occupant(back) <input type="checkbox"/> Occupant(unkn.) <input type="checkbox"/> Pedestrian <input type="checkbox"/> Non Vehicle <input type="checkbox"/> Skate board / Roller-skater <input type="checkbox"/> Unknown	
<b>Death Date/Time:</b> <input type="checkbox"/> CTB <input type="checkbox"/> Confirmed			<b>Time Accuracy:</b> <input type="checkbox"/> Correct <input type="checkbox"/> Minutes Estimated <input type="checkbox"/> Hours/Minutes Estimated <input type="checkbox"/> Unknown/ Missing	<b>PMHx:</b> <input type="checkbox"/> NONE <input type="checkbox"/> Smoking: <input type="checkbox"/> Heart Disease <input type="checkbox"/> Circulation Problems <input type="checkbox"/> HTN <input type="checkbox"/> Lung Disease <input type="checkbox"/> Anemia/ Bleeding d/o <input type="checkbox"/> Transfusion Reaction <input type="checkbox"/> Surgery <input type="checkbox"/> Anesthesia Reaction <input type="checkbox"/> Neurological Disease <input type="checkbox"/> Seizures <input type="checkbox"/> Stomach/GI Problems <input type="checkbox"/> Liver Disease <input type="checkbox"/> Diabetes <input type="checkbox"/> STD <input type="checkbox"/> Trauma <input type="checkbox"/> Psychological d/o <input type="checkbox"/> Kidney Disease <input type="checkbox"/> Arthritis/ M.Skeletal <input type="checkbox"/> Infectious Disease <input type="checkbox"/> Cancer <input type="checkbox"/> Chronic Pain <input type="checkbox"/> Eye Problems <input type="checkbox"/> Etoh Abuse <input type="checkbox"/> Drug Abuse <input type="checkbox"/> Other	
<b>Age:</b>		<b>Consent:</b> Next of Kin initials: _____	<b>Type of Head Injury:</b> <input type="checkbox"/> Other <input type="checkbox"/> Moderate (GCS 9-12) <input type="checkbox"/> Severe	<b>Place of Injury:</b> <input type="checkbox"/> Home <input type="checkbox"/> Work/ School <input type="checkbox"/> Street/ Highway <input type="checkbox"/> Recreational area <input type="checkbox"/> Hospital <input type="checkbox"/> Other _____ <input type="checkbox"/> Unknown	
<b>Gender:</b> <input type="checkbox"/> Female <input type="checkbox"/> Male			<b>Mechanism of injury:</b> (circle one) Automobile, Truck, Bus, Off-Road Vehicle, Recreation Vehicle, Construction/ Industrial/ Farm Machinery, Motorcycle, Moped, Bicycle, Skateboard, Roller Skates, Train, Plane, Boat, Fall/ Jump, Sports, Falling Object, Assault, Knife, Explosion, GSW, Unorganized Sports, Other, N/A, Unknown Other _____	<b>Arrived from:</b> <input type="checkbox"/> Scene <input type="checkbox"/> Hospital	
<b>Race:</b> <input type="checkbox"/> American Indian, Alaskan <input type="checkbox"/> Asian, Pacific Islander <input type="checkbox"/> Black <input type="checkbox"/> Hispanic <input type="checkbox"/> White <input type="checkbox"/> Other		<b>Cooling Time Started:</b>	<b>Transport:</b> <input type="checkbox"/> Helicopter <input type="checkbox"/> Ambulance <input type="checkbox"/> Other		
<b>Height (inches):</b>			<b>Cooling Time Achieved:</b>	<b>Contributing Factors:</b> (No, Yes, N/A, Unknown) <b>Safety Belt</b> _____ <b>Helmet</b> _____ Drugs _____ Other _____ Work Related _____ Suicide _____ Child Abuse _____ Spouse Abuse _____	
<b>Weight (lbs):</b>		<b>GCS:</b>			
<b>Zip:</b>		<b>GCS Date/Time:</b> _____			
<b>Marital Status:</b> <input type="checkbox"/> Single <input type="checkbox"/> Married <input type="checkbox"/> Unknown		<b>Post Op GCS:</b>			
<b>Other Notes:</b>					
Time Paged:		Contact Person/ Relationship:			
Arrived:		Numbers:			
IV Fluids:					

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