INFORMED CONSENT FORM TO TAKE PART IN RESEARCH

HypOthermia for Patients requiring Evacuation of Subdural Hematoma:
a Multicenter, Randomized Clinical Trial
"The HOPES Trial"
HSC-MS-12-0762

The following information applies to the research subject. If the subject is unable to provide consent upon arrival at the hospital, consent will be sought from the subject's legally authorized representative. The terms "you" and "your" in the procedure section refers to the research subject.

INVITATION TO TAKE PART

You are invited to allow your family member to take part in a research project called, "HypOthermia for Patients requiring Evacuation of Subdural Hematoma: a Multicenter, Randomized Clinical Trial" (*The HOPES Trial),* conducted by Dr. Dong Kim, of the University of Texas Health Science Center at Houston and collaborators. For this research project, he will be called the Principal Investigator or PI.

Your decision to take part is voluntary. You may refuse to take part, or choose to stop taking part, at any time. A decision not to take part in or to stop being a part of, the research project will not change the services available to you from your physician, Memorial Hermann Hospital, Mischer Neuroscience Associates, The University of Texas Health Science Center at Houston or collaborating institutions.

You may refuse to answer any questions asked or written on any forms. This research project has been reviewed by the Committee for the Protection of Human Subjects (CPHS) of the University of Texas Health Science Center at Houston as HSC-MS-12-0762.

PURPOSE

Your family member is invited to join this research study because they have had a head injury, with brain bleeding, which requires surgery.

The purpose of this research study is to find out if therapeutic hypothermia improves outcome following traumatic brain injury (TBI) which requires surgery. Therapeutic hypothermia means to lower the body temperature below normal, in this case to about 33°C or 91.4°F (normal body temperature is about 37°C or 98.6°F). This study will also look at the safety of therapeutic hypothermia in the management of brain injury and look at the effect of hypothermia in reducing

the occurrence of depolarization in the brain. Depolarization in the brain are short-circuits (electrical failures) that occur in a specific area of injury and result in dampened brain waves, which has been shown to be harmful. The study will also test to see if the levels of certain proteins in the blood are lowered by hypothermia. The catheters used for temperature management in this study have been cleared for use by the FDA. However, therapeutic hypothermia in traumatic brain injury has not been approved as a treatment by the FDA.

This is a collaborative, multi-center study with three locations participating across the country. The study will enroll up to a total of 350 people nationally. [redacted]

PROCEDURES

- What to expect as a subject:
  If you agree to allow your family member to take part in this study, your family member will have the following procedures:
  - If you have been assigned to the normothermia treatment, you will receive 1-3 liters of room temperature IV fluids. If you have been assigned to the hypothermia treatment, you will receive 1-3 liters of chilled IV fluids to start lowering your body's temperature. (You will receive IV fluids and a catheter as part of your standard treatment even if you are not in the study.)
  - A catheter will be inserted into your femoral (leg) vein. Your temperature will be maintained by a temperature-controlling unit, the CoolGard 3000 or Thermogard XP. If you were placed in the hypothermia treatment group, you will be cooled to a temperature of 35°C (95°F) prior to surgery, and then kept at a temperature of 33°C (91.5°F) for at least 48 hours, and up to 5 days. You may have other cooling used if the catheter needs to be removed before time for re-warming. You will be re-warmed slowly and carefully.
  - We will take blood three times to check the levels of certain proteins which may be helpful in predicting or assessing outcome. Genetic material (buffy coat in the blood sample) will be banked for future research. Blood samples will be taken at 3 times:
    - Time 1: within 6 hours of injury (one tablespoon.)
    - Time 2: after surgery (one tablespoon.)
    - Time 3: 5-14 days after injury, or at discharge, whichever comes first (one tablespoon.)
  - If you have a ventricular drain (a catheter inserted in the brain to monitor brain pressure) in place, we will collect samples as available (about one teaspoon each, about one Tbsp. total) of your cerebrospinal fluid (CSF) as well.
  - Following surgery to remove the blood clot from your brain, a strip of electrodes may be placed on the brain to monitor electrical activity. Brain activity will be recorded throughout the period of temperature control and when monitoring of pressure in the brain is clinically indicated.
  - You will be assessed 4-6 weeks after your date of injury using the Disability Rating Scale (DRS), and then again at 6-months (±2 weeks) using the Glasgow Outcome Scale Extended (GOSE). These are standard surveys used in TBI and will only take about 15 minutes of your time.

If you agree to take part in this study you will be randomized (like flipping a coin) to receive hypothermia treatment (cooled below normal body temperature) or normothermia treatment (maintained at normal body temperature). It is not known whether hypothermia treatment will be of benefit. For this reason, some study participants must receive the

normothermia treatment. This will allow a careful comparison to study the benefits and side effects of the hypothermia treatment. There is a 50% chance you will receive the hypothermia treatment and a 50% chance that you will receive the normothermia treatment. You will not know if you are receiving the hypothermia treatment or normothermia treatment until after you are put in the study group.

- For venipunctures for blood samples:

You will have about 1 Tbsp. of blood drawn from an existing line, or a vein in your arm (if there are no existing lines), three different times during your treatment. The total amount of blood withdrawn during your participation will be about 3 tablespoons.

Schedule of Evaluations and Implementations

Procedure	Arrival at MHH	During Surgery	After Surgery	48hrs-5 days	5-14 Days	4 Weeks After	6 Mos. After
Medical History	Standard care						
Physical Exam	Standard care						
Vital Signs	Standard care						
Head CT	Standard care		Standard care				
Samples	**X**		**X**		**X**		
Maintenance of Temperature Control	**X**	**X**	**X**				
Re-warming in Hypothermia Patients				**X**			
Brain activity monitoring			**X**	**X**	**X**		
Outcome evaluations						**X**	**X**

I DO_____DO NOT _____want my blood and genetic samples saved for this medical research.

I DO_____DO NOT _____want my blood and genetic samples saved for future medical research.

I DO_____DO NOT_____ want to be contacted for future research.

I DO_____DO NOT_____ agree to allow the data to be used for this research.

TIME COMMITMENT

The total amount of time you will take part in this research study is 6 months, including:

- Duration of pre-operative and post-operative stay in hospital
- Two follow-up visits; one at 4 weeks after your injury, and one at 6 months (±3 weeks) after your injury
- Your samples will remain indefinitely in the Neuroscience Research Repository at the University of Texas Health Science Center at Houston for future research.

BENEFITS

The research in this study may or may not help you personally, but it may provide more knowledge about the care of traumatic brain injury patients. This information may help future patients with the knowledge of preventative treatments and more useful therapy.

RISKS AND/OR DISCOMFORTS

While on this study, you are at risk for side effects. The study team will discuss these risks with you. This study may include risks that are unknown at this time.

Therapeutic Hypothermia: complications due to hypothermia include irregular heart rhythms, risk of infection, bleeding, blood clotting, elevated blood sugar, and shifting of electrolyte levels.

Blood Draw: You may experience slight pain, discomfort, bruising, or in rare cases, infection at the site the blood was taken from your arm, if you don't have an existing line from which we may collect blood samples.

Confidentiality: Possible risk of breach of confidentiality

Brain activity monitoring: The risk of infection or bleeding is approximately 1-5%, but no such complications have been observed previously in similar patients who have undergone this procedure. The electrode strip will be removed at the bedside by the neurosurgeon. There is approximately a 1-2% risk for difficulty in removing the strip. If this should occur, the scalp incision may need to be extended a small amount to allow for removal.

ALTERNATIVES

The only alternative is not to take part in this study.

STUDY WITHDRAWAL

Your decision to take part is voluntary. You may refuse to take part, or choose to stop taking part, at any time. A decision not to take part in or to stop being a part of, the research project will not change the services available to you from your physician, Memorial Hermann Hospital-Texas Medical Center, Mischer Neuroscience Associates, The University of Texas Health Science Center at Houston or collaborating institutions.

Your doctor or the sponsor can stop the study at any time for any of the following reasons: if you have an adverse effect from the hypothermia treatment, if you need a treatment not allowed in this study, if the study is stopped by the FDA or the sponsor ahead of schedule, or for any other reason. Should the study be stopped, your study doctor will discuss other options for treatment.

If you decide to stop participating in the study early, controlled re-warming must be completed for your safety. If you stop study participation, we will continue to monitor you for your safety, including collecting blood samples and information about adverse events.

During and after the study, you will have the right to have your samples (blood and/or CSF) destroyed at any time. If you decide to have your sample destroyed, any data that was acquired or analysis that was done before the request cannot be removed. However, no further testing will be done, and all remaining samples will be destroyed.

Please note that you have the right to access your genetic data and to ask for correction as allowed by national law. Otherwise, University of Texas Health Science Center at Houston is responsible for the destruction of the sample at the end of the storage period.

IN CASE OF INJURY

If you suffer any injury as a result of taking part in this research study, please understand that nothing has been arranged to provide free treatment of the injury or any other type of payment. However, all needed facilities, emergency treatment and professional services will be available to you, just as they are to the community in general. You should report any injury to Dr. [redacted] and to the Committee for the Protection of Human Subjects at (713) 500-7943. You will not give up any of your legal rights by signing this consent form.

COSTS, REIMBURSEMENT AND COMPENSATION

There is no monetary cost to you for taking part in this research study. The only compensation for this study is parking validation upon your visits at the clinic to be evaluated at 4 weeks and 6 months (±3 weeks). It is possible that your biological samples may be used to develop new medical products in the future, but you will receive no financial benefit. The samples will be the property of The University of Texas Health Science Center at Houston. Neither you nor the researchers have any ownership of proprietary interest in the samples. If there is a potential for commercial value that could be derived from the research, you will not have any rights or control over the genetic sample collected.

You are responsible for the costs of your regular care. If you receive a bill that you believe is related to your taking part in this research study, please contact [redacted] with questions.

CONFIDENTIALITY

Please understand that representatives of the Food and Drug Administration (FDA); the Committee for the Protection of Human Subjects; the Data and Safety Monitoring Committee; the University of Texas Health Science Center; [redacted] (Research Monitor); [redacted] (Data Monitor); and the sponsors of this research may review your research and/or medical records for the purposes of verifying research data, and will see personal identifiers. Representatives of the Department of Defense are authorized to review research records as part of their responsibility to protect human research volunteers. However, identifying information will not appear on records retained by the sponsor, with the exception of the date of birth, subject initials, and treatment/service dates. You will not be personally identified in any reports or publications that may result from this study. There is a separate section in this consent form that you will be asked to sign which details the use and disclosure of your protected health information.

The human derived biological samples (HDBS) bank administered by the University of Texas Health Science Center Houston (UTHSC-H) will remain with UTHSC-H unless the UTHSC-H agrees to release and/or transfer the samples. Please be aware that if the PI leaves the University, the samples within the HDBS bank will remain the property of UTHSC-H. The University's ownership includes the right to transfer ownership to other parties, including commercial sponsors. The PI does not have any ownership or proprietary interest in the HDBS bank.

You will not receive information about your samples. You will not be personally identified in any results that are published regarding the analysis of your samples.

The University of Texas Health Science Center will require anyone who works with your samples to agree to hold the information and any results in confidence.

Clinical Trials.Gov Language:
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

NEW INFORMATION

While taking part in this study, the study team will notify you of new information that may become available and could affect your willingness to stay in the study. They will notify you of this information during your follow-up visits at 4 weeks and 6 months after surgery and via phone call or email thereafter.

QUESTIONS

If you have questions at any time about this research study, please feel free to contact Dr. Kim at [redacted] You can contact the study team to discuss problems, voice concerns, obtain information, and offer input in addition to asking questions about the research.

Authorization for the Use and Disclosure of Protected Health Information for Research

University of Texas Health Science Center at Houston and/or Memorial Hermann Healthcare System (MHHS)

NAME OF SUBJECT: _____ DATE OF BIRTH _____

I hereby authorize the following Health Care Provider to release the following information from the medical records of the patient identified above to The University of Texas Health Science Center at Houston (UTHSCH) or Memorial Hermann Hospital System (MHHS) and specifically to the Principal Investigator listed below and the study research staff.

I understand I have the right to revoke this authorization in writing at any time except to the extent that action has been taken in reliance upon it. I understand that I may revoke this authorization by sending, via mail or facsimile, a written notice to the following individuals/organizations stating my intent to revoke this authorization

Study Title: Therapeutic Hypothermia for Traumatic Brain Injury Patients Requiring Evacuation of Acute Subdural Hematoma: a Multicenter, Randomized Clinical Trial

Principal Investigator: Dong Kim, MD

Address: The Vivian L, Smith Department of Neurosurgery
University of Texas Health Science Center at Houston
6431 Fannin Street, MSB 7.146
Houston, TX 77030
Phone: [redacted] **Fax**: [redacted]
If applicable complete the following:

☐ The University of Texas Health Science Center at Houston

Address: Mischer Neurosurgical Associates
6400 Fannin Street, Suite 2800
Houston, TX 77030
Fax: [redacted]

☐ Memorial Hermann Healthcare System

Privacy Officer
Memorial Hermann Healthcare System
Address: 909 Frostwood Southwest Freeway
Houston, Texas 77074
Fax: (713) 338-4542

Other Known Health Care Provider (Provide Information)
Address: _____ Phone: _____
Fax:_____

The information to be released to the Principal Investigator will include (Please Check appropriate box)
☐ Complete Clinical Records
☐ Other

UTHealth The University of Texas Health Science Center at Houston
IRB NUMBER: HSC-MS-12-0762
IRB APPROVAL DATE: 04/11/2017

Please specify portions of the records to be released:

_____

I understand that the Principal Investigator may **disclose** information to the Committee for the Protection of Human Subjects (CPHS) and the Clinical Research Billing Compliance Office for the purposes of verifying research data.

In addition, I understand that the Principal Investigator listed above may disclose the information to the following:

List Names here:

- [redacted]
- Food and Drug Administration
- Data Safety Monitoring Board
- Neuroscience Research Repository investigators and study team members
- National Institute of Neurological Disorders and Stroke (NINDS)
- Office for Human Research Protections (OHRP)
- [redacted]
- [redacted]
- [redacted]
- [redacted]

The information that may be **disclosed** to (shared with) the parties may include (Please check appropriate box)

☒ Complete Clinical Records
☐ Other
Please specify portions of the records to be released:_____

The information that may be **retained** by the parties may include (Please check appropriate box)

☒ Complete Clinical Records (must be de-identified)
☐ Other
Please specify portions of the records to be released: _____

I understand that UTHSCH or MHHS personnel who obtain access to my health information as part of this research study may not use the information for purposes other than this study, except as otherwise permitted by law. I understand that to the extent any Recipient of this information, as identified above, is not a "covered entity" under Federal or Texas privacy law, the information may no longer be protected by Federal and Texas privacy law once it is disclosed to the Recipient and, therefore, may be subject to re-disclosure by the Recipient.
I understand that the University of Texas Health Science Center (UTHSCH) or Memorial Hermann Hospital System (MHHS) may not withhold or condition treatment based on my completion of this authorization form.
I understand that the records used and disclosed pursuant to this authorization form may include information relating to: Human Immunodeficiency Virus (HIV) infection or Acquired Immunodeficiency Syndrome (AIDS); treatment for or history of drug or alcohol abuse; or mental or behavioral health or psychiatric care.
In the case of an adverse event related to or resulting from taking part in this study, I authorize the researchers listed above to access test, treatment and outcome information about the adverse event from the treating facility.

Unless otherwise revoked, this authorization will expire on the 180th day after the signing or as otherwise specified below:

☐ Authorization will expire on the 180th day after signing this form.
☐ Authorization will expire on:
☐ Expiration date:_____

OR

☐ Authorization will expire (enter number of years) __15___years after the end of the study.

Special Instructions: _____

SIGNATURES

Sign below only if you understand the information given to you about the research and choose to take part. Make sure that any questions have been answered and that you understand the study. If you have any questions or concerns about your rights as a research subject, call the Committee for the Protection of Human Subjects at (713) 500-7943. You may also call the Committee if you wish to discuss problems, concerns, and questions; obtain information about the research; and offer input about current or past participation in a research study. If you decide to take part in this research study, a copy of this signed consent form will be given to you.

_____

Printed Name of Subject

_____

Printed Name of Subject or Legally Authorized Representative

_____ _____ _____

Signature of Subject or Legally Authorized Representative Date Time

_____

Printed Name of Person Obtaining Informed Consent

_____ _____ _____

Signature of Person Obtaining Informed Consent Date Time

CPHS STATEMENT: This study (HSC-MS-12-0762) has been reviewed by the Committee for the Protection of Human Subjects (CPHS) of the University of Texas Health Science Center at Houston. For any questions about research subject's rights, or to report a research-related injury, call the CPHS at (713) 500-7943.