

**CONSENT TO TAKE PART IN A CLINICAL RESEARCH STUDY
AND
AUTHORIZATION TO DISCLOSE HEALTH INFORMATION**

**ADULTS/SUBJECTS WHO TURN 18/PARENTAL/GUARDIAN PERMISSION
& ASSENT FOR AGES 14 TO AGE OF MAJORITY**

Study Title: "Brain Oxygen Optimization in Severe Traumatic Brain Injury - A multi-center, randomized, blinded-endpoint, comparative effectiveness study of goal-directed critical care based upon monitoring of brain tissue oxygen and intracranial pressure versus monitoring of intracranial pressure alone in patients with severe traumatic brain injury"

Granting Agency: The National Institute of Neurological Disorders and Stroke (NINDS)

Protocol Number: BOOST-3

**Principal Investigator:
(Study Doctor)** «PiFullName»

Telephone: «IcfPhoneNumber»

**Additional Contact(s):
(Study Staff)** «AdditionalStaffMemberContacts»

Address: «PiLocations»

This form is for use in a research study that involves participants who are unconscious or in coma, and do not have the capacity to consent to take part in the study. You are the legally authorized representative of the patient. In cases where the participant's representative gives consent, the participant should be informed about the study to the extent possible if the participant regains consciousness. During the course of the study, if the subject regains the capacity to consent, informed consent will be obtained from the subject and the subject offered the ability to leave the study if desired.

SUMMARY OF KEY INFORMATION

Your family member (or a person you represent) has had a severe traumatic brain injury (TBI). He or she may be eligible to participate, or continue to participate, in a research study. The study is to compare two ways of treating patients with brain injury. Physicians do not know which standard of care treatment is better. Neither treatment being studied are investigational. We are talking with you because patients with severe TBI are unconscious or in a coma; and they cannot tell us if they want to participate in a study. You are the patient's representative. In an effort to provide immediate emergency care, the person you represent may have already been entered in this study. If not, we are asking you to consent or refuse consent for his or her participation. If the patient was already entered in the study, we are asking you for your consent to allow them to continue or to stop participation in the study. The remainder of this document should help you in this decision.

Participants in this study are placed at random, that is by chance, in one of two groups. One group has medical care based on monitoring of pressure in the brain (intracranial pressure or ICP) alone. The other group has medical care based on both ICP and the amount of oxygen in the brain (brain tissue oxygen or PbtO₂). It is unknown if measuring and treating low brain oxygen is more effective, less effective, or the same as monitoring and treating high brain pressure alone. Treatment differs by group because doctors make decisions guided by ICP and PbtO₂ goals. These decisions include the kinds and doses of medications given. They also include the amount of fluids given by vein. Other treatments that may differ can also include changing ventilator (breathing machine) settings, blood transfusions, and other parts of medical care. ICP and PbtO₂ are monitored by small sensor probes placed in the brain through one or two small holes made in the skull. Placing one or both of these probes is standard care for people with severe TBI. They are placed within hours of arrival at the hospital. Those in the study will have both probes placed.

After the initial hospitalization, we will contact participants or their caregivers about once per month for 5 months to see how they are doing. A study team member will schedule a follow up visit to the clinic about 6 months after the injury to learn about how the participant is doing. The study team will review the participant's medical records while they are in the study as needed. About 1,000 participants will be enrolled at about 45 hospitals.

Participation in the study will help doctors learn if one way of treating future victims of TBI is better. Participants may or may not directly benefit from being in the study. Some participants may benefit directly if recovery turns out to be more likely with the management they receive. Participation may also have risks. Some possible risks are currently unforeseeable. Known risks from study participation include accidental release of private information. Other risks may include bleeding around the sensors, infection, lung problems, or other medical complications. Risks will be discussed later in this consent form.

Participation in the study, or ongoing participation if your family member was already enrolled before we could reach you, is voluntary. The alternative to being a part of this study is to receive the usual standard of care. Usual care may be either of the ways of treating patients being compared in the study. Usual care often varies based on the injury, the choice of the doctor, or the treating hospital. There is no penalty for choosing not to participate. A participant can withdraw from the study at any time.

Medical records and data collected in the study will remain as private as possible. Participants' records may be viewed by the study team here or from the study coordinating centers. Records may also be seen by those responsible for reviewing the safety and conduct of the study. This oversight is provided by this institution and by government regulatory and funding agencies.

There is no payment or compensation for being in the study. There is no cost to being in the study. Charges for all standard medical care will be billed the same way whether or not someone is in the study.

Please contact us for any questions about the research, participants' rights, or other concerns.

- Please carefully read this form, additional detail about each item just described is found below
- Please listen to the study team explain the study and this form to you
- Please ask questions about anything that is not clear

If you consent, you will be asked to sign and date this form.

MORE DETAILED INFORMATION

What is the purpose of this research study?

The purpose of the research study is to learn if either of two strategies for monitoring and treating patients with TBI in the intensive care unit (ICU) is more likely to help them get better. Both of these alternative strategies are used in standard care. It is unknown if one is more effective than the other. In both strategies, doctors monitor the patient's brain and modify the medical care provided in order to try to improve some measure of the brain's health. However, it is not known which measure of the brain's health, intracranial pressure or oxygen level, is more important. In one strategy doctors concentrate only on preventing high ICP (intracranial pressure) caused by a swollen brain. In the other strategy doctors try to prevent high ICP, and also try to prevent low PbtO₂ (brain oxygen). Some hospitals and doctors tend to use one or the other strategy more often. It is unknown if measuring and treating low brain oxygen is more effective, less effective, or the same as monitoring and treating high brain pressure alone. The results of this study will help doctors discover if using both of these methods is better than using one alone in treating TBI.

Why is this an important question to study?

When a person has a TBI, their injured brain can swell over a period of hours or days. If the brain swells too much, the pressure in the skull increases and becomes dangerous, causing further injury to the brain. To try to prevent this, doctors usually insert a device, an ICP probe, into the brain through a hole in the skull of people with severe TBI. An ICP monitor connected to the probe measures the pressure inside the skull. Most doctors agree that it is important to measure and prevent high ICP.

Patients with injured brains also suffer additional injury to the brain if the amount of oxygen in the brain gets too low. Some doctors also insert a second device, a PbtO₂ probe, in the brain through the same or a second hole in the skull to measure brain tissue oxygen. A PbtO₂ monitor connected to the probe measures how much oxygen is in a small area of the brain near the tip of the probe. Doctors disagree about whether monitoring oxygen levels is helpful or necessary.

Both monitoring devices are approved by the US Food and Drug Administration (FDA) and Health Canada for patients with TBI. Both are commonly used. The ICP and PbtO₂ goals guided by these monitors are used to help doctors adjust their treatment choices. Treatments include kinds and doses of medications and the amount of intravenous fluids given, ventilator (breathing machine) settings, need for blood transfusions, and other medical care. Each of these treatment decisions is intended to improve outcomes. However, each treatment decision also involves potential risks. Different treatment decisions may result in different risks. This study will also help doctors better understand these risks.

This study is funded by the National Institutes of Health because it answers questions important to the care of patients with TBI.

How long will the participant be in the study? How many people will be in the study?

- Participants are in the study for about 6 months. The treatments being studied all occur in the first 5 days.
- About 1,000 participants will be enrolled at about 45 hospitals.
- We will call participants (or their caregivers) about 5 times after their injury. We will call about once each month for 5 months. Each phone call will last about 15 minutes. During the phone call, we will ask how they are doing, if they are having any additional problems, and if any of their contact information has changed.
- We will ask the participant to come in for a study visit about 6 months after their brain injury. If they are not well enough to travel, a member of the study team can visit them where they are living, if they agree. The visit will take about 1 hour. During the visit, a study team member will ask questions about the participant's recovery. There will be a questionnaire and some pencil and paper exercises. There are no risks anticipated from this visit.
- If the participant is unable to have an in-person interview, a telephone interview with the participant or caregiver can be done instead. If possible, the telephone interview will collect the same information as the visit except for the pencil and paper exercises. It may also take up to 1 hour.
- Translators will be available for calls and visits with individuals whose preferred language is not English.

What happens in this study?

- All participants will have both an ICP probe and a PbtO2 oxygen probe placed.
- Participants will have an equal chance (like the flip of a coin) of being allocated to one of the two groups. The groups determine which information about the brain will be used to guide medical care.
 - Group 1: medical care guided by ICP monitoring (the PbtO2 monitor is covered and not used)
 - Group 2: medical care guided by ICP and PbtO2 monitoring
- This random (like the flip of a coin) allocation to one group or another is research.
- Medical care of the participant will be guided by this group allocation (which group the participant is in) for 5 days.
- Medical care of the participant affected by group allocation might include the choices and doses of medications and the amount of intravenous fluids given, how the participant's ventilator is adjusted, the need for blood transfusions, and other components of ICU care.
- Other than which monitoring information is used to guide care in the first 5 days, all participants receive usual care. Use of monitoring beyond 5 days is also based on usual care.
- Doctors caring for participants in group 1 will make decisions based on the ICP monitor. They will not see the information from the PbtO2 monitor. They will not make any decisions based on PbtO2 information. Having a PbtO2 monitor, but not using the information to guide care is part of the research.
- One or both probes may be removed before 5 days if there is a clinical reason to do so. This may include the participant waking from coma, infection of the probe, or 3 or more days without abnormal readings on the monitors.
- Information is collected for the study from participants' medical record, diagnostic images, and monitors. Information collected includes the condition of the patient and the treatments being provided.

- We will visit the participant daily during the first 5 days in the ICU, and periodically while in the hospital. We will review the medical record at these times, at discharge, and at any return visits during participation.
- Contact information for the participant, you, family members, close friends, or caregivers is collected in order to arrange follow up during the study. These include phone numbers, email and mailing addresses.

What risks may participants experience?

There are potential clinical risks to all the treatments used in the medical care of patients with severe TBI. These risks are the same whether or not they participate in the study. Participation in research may also have risks.

Clinical risks potentially related to the monitors and treatments include, but are not limited to, the following:

- Pneumonia (infection of the lung) is common in those with severe TBI (about 1 in 4), and may rarely be increased because of efforts to optimize PbtO₂ (fewer than 5 in 100).
- Lung injury, sometimes related to ventilator settings or the amount of intravenous fluids given, which may be affected by brain monitoring, is also common (about 1 in 20).
- Severe sepsis, a dangerous infection spread in the blood, is common (about 1 in 20), usually unrelated to monitoring.
- Placement or removal of probe can sometimes cause slight bleeding at the site of insertion (fewer than 2 in 100). Rarely, a medicine or procedure to reduce bleeding might be used (fewer than 1 in 5000).
- Infection in the brain, possibly related to brain probe placement, is rare (fewer than 1 in 5000).

Risks related to being a study participant include:

- Breach of confidentiality is a rare risk of participation in research studies (fewer than 1 in 10,000).
- If you request it, you may be emailed a PDF copy of this signed and dated consent form. There may be risks of loss of privacy and confidentiality if the PDF copy of this consent form is viewed and/or stored on a personal electronic device (PED), especially if that PED is shared with other users or is lost, hacked, or subject to a search warrant or subpoena. Also, the PDF copy of the consent may not be able to be permanently removed from a PED.

The researchers have taken steps to minimize these risks. The study team will monitor closely for these possible risks and complications will be treated if needed.

To reduce any potential risk to an unborn child, women of childbearing potential will have a pregnancy test and if pregnant, will not be included in this research study.

As with any research study, there may be additional risks that are unknown or unexpected.

What is the possible benefit?

The participant may or may not benefit from being in this study. Some participants may benefit directly if recovery turns out to be more likely with the management they receive. Discovery that one strategy or the other helps traumatic brain injury patients recover with less disability will be an important advancement in the treatment of future patients with brain injury.

What is the alternative to participating in this study?

Participation, or ongoing participation, in this study is voluntary. The alternative to participating in the trial is usual care. Usual care may be medical care guided by ICP monitoring or it may be medical care guided by ICP and PbtO2 monitoring. The usual care offered may depend on the treating hospital, opinion of the doctors caring for the individual, or upon characteristics of the patient or their injury. There is no penalty for choosing not to participate. The participant may withdraw from the study at any time, either by his/her choice or at the direction of the participant's legally authorized representative. Choosing not to participate, not to continue participation, or choosing to withdraw will not alter the usual care available. Nor does it alter or waive any legal rights or benefits.

What if new information becomes available?

We will provide any new information that may affect a participant's willingness to continue in the study. Participants may be contacted about future available studies. We may also contact participants with periodic updates about the study. We may also contact participants after the trial has been completed to share results from the study.

AUTHORIZATION TO DISCLOSE HEALTH INFORMATION**How will personal information be protected?**

The study investigator and his/her collaborators will consider the participants' personal information confidential to the extent permitted by law. "Personal Information" means information that can be used to identify the participant or health information about the participant. This includes name or initials, date of birth, gender, ethnic origin and medical and health-related information such as blood tests, diagnostic imaging and results, the results of physical examinations, medical history and hospital records, and information directly observed in the study.

Information about the participant collected for the study may be stored electronically or on paper. The information stored on the computer is kept in password protected files that are maintained on password protected computers. The information stored on paper is stored in a locked file cabinet in a locked office. Only the members of the study team and the persons and groups listed below will have access to the participants' medical information for this study.

The government agencies responsible for making sure that studies are conducted and handled correctly, and other organizations involved in this research study may look at the participant's study records in order to perform their duties. These include: the US National Institutes of Health (NIH), the US Office for Human Research Protections, the US Food and Drug Administration (FDA), Health Canada, researchers from University of Pennsylvania and the University of Pittsburgh, representatives from The Strategies to Innovate Emergency Care Clinical Trials Network (SIREN) Clinical Coordinating Center at the University of Michigan, representatives from the Data Coordination Unit at the Medical University of South Carolina, the Central Institutional Review Board, and/or other agents of the study who will be bound by the same provisions of confidentiality. Information from this study may be submitted to the US Food and Drug Administration (FDA) and Health Canada.

To help us protect the participant's privacy, this research is covered by a Certificate of Confidentiality from the US National Institutes of Health. With this Certificate, the investigators may not disclose or use information, documents, or biospecimens that may identify the participant in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, in the US unless the participant has consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not

connected with the research except, if there is a federal, state, or local law that requires disclosure (see below); if the participant has consented to the disclosure, including for the participant's medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

Disclosure is required, however, for audit or program evaluation requested by the NIH or when required by the FDA or Health Canada. A Certificate of Confidentiality does not prevent the participant from voluntarily releasing information about themselves or their involvement in this research. If the participant wants research information released to someone, the participant must provide consent to allow the researchers to release it. The certificate covers disclosures involving participants enrolled in Canada in US legal proceedings, but does not cover disclosures in proceedings outside the US.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of, for instance, child abuse or neglect, harm to self or others, and communicable diseases.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

Although every effort will be made to maintain confidentiality of the participant's medical and health records, absolute confidentiality cannot be guaranteed. We will use a study number rather than the participant's name on study records where we can. The participant's name and other facts that might point to the participant will not appear when we present this study or publish its results. Viewing or storing this electronic informed consent form on a personal electronic device may allow information provided on this form (such as names and email addresses) to be inadvertently shared with others if the device is lost, hacked, or otherwise compromised.

When ready to leave the hospital, typically well after the 5 days of study treatment is complete, the participant may be discharged to a rehabilitation or nursing facility. The participant might also be discharged home and then readmitted to another medical facility later. Your signature on this document authorizes those facilities to release medical records to the researchers and research staff of this study for the 6 months the participant is in the study.

We will keep any records that we produce private to the extent we are allowed or required by law. The participant's records will be kept for as long as necessary for purposes of the research study.

The study doctor and treating institution are required by law to protect the study participants' health information. With this form, you authorize the study doctor to use and disclose the participant's health information, as described in this section, in order to conduct this research study. You have the right to revoke this authorization, at any time, and can do so by writing to the study doctor at the address on the first page. Even if you revoke the authorization, the study doctor and/or sponsor may still use health information they have collected about the study participant, if necessary, for the conduct of the study. However, no new information will be collected.

Your authorization does not have an expiration date unless indicated elsewhere. You do not have to sign this information and consent form, but if you do not, the person you represent will not be able to take part in this research study. Those persons who receive the participant's health information may not be required by US Federal privacy laws (such as the Privacy Rule)

to protect it and may share the information with others without your permission, if permitted by laws governing them.

By signing this information and consent form, you consent to the collection, access, use and disclosure of the participant's information as described above. State law or the enrolling institution may require an additional separate form on which you can authorize sharing of the participant's health information. If so, you will have to sign both forms for your authorization to be valid.

How may the participants' data and samples be shared?

US Federal rules require that data be securely stored in the Federal Interagency Traumatic Brain Injury Research (FITBIR) informatics system where it can also be accessed by researchers in a de-identified manner. For more information see the website <http://fitbir.nih.gov>

Will the participant have to pay anything?

There is no additional cost to participate in the study. Charges for all standard medical care will be billed in the same manner regardless of participation. Participants who receive the brain oxygen probe in the study will not be charged for it, nor will a public health plan, or the participant's private medical insurer (if any). Funds are not available to cover the costs of any ongoing medical care and participants remain responsible for the cost of non-research related care. For questions about the participant's medical bills relative to research participation, contact the study investigator listed on this form.

Will the participant be paid for being in the study?

No. There will not be any payment to the participant for being in this study.

What if the participant is injured as result of being in this study?

If a participant is injured or becomes ill from participating in the study, medical treatment will be available at this institution or elsewhere consistent with the care provided for any medical problem. Payment for this care will be billed the same as any other care for any medical problem. If the hospital at which the participant was enrolled has any additional answers to this question, this information is found at the bottom of this form.

In the event that the participant suffers injury as a result of their participation in this research study, no compensation will be provided to the participant by the granting agency (National Institute of Neurological Disorders and Stroke), the treating institution, or the researchers. The participant still has all of their legal rights. Nothing said here about treatment or compensation in any way alters the participants' right to recover damages.

Is there anything else I need to know?

Continued participation in this study is voluntary. The participant may withdraw from the study at any time and for any reason without penalty. The researcher may discontinue participation if the study is discontinued or suspended. No more information will be collected about a participant after they withdraw from the study or complete their participation.

You may ask to stop having the study affect the participant's medical care. If so, usual care will resume. Usual care is based on the individual patient and their injury, the opinion of the treating doctors, and the treating institution. Usual care may be medical care guided by ICP alone, or medical care guided by ICP and PbtO2 monitoring.

Doctors caring for the participant during this hospitalization may also be researchers in this study. If so, the doctors are interested both in the participant's medical care and in the conduct of this research. There is no obligation to participate in any research study just because it is offered by the participant's doctors.

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.

What if I have questions?

You or the participant may ask and will receive answers to any questions you have during the course of the study. For any questions regarding this study or if the participant experiences any side effects or medical problems, contact the site researcher listed on this form.

Advarra serves as the Central Institutional Review Board (CIRB) for this study. The CIRB is not part of the research or the research team. Please contact Advarra, if you:

- have questions about your role and rights as a research participant;
- wish to obtain more information about clinical research in general;
- have concerns, complaints or general questions about the research, or;
- wish to provide input about the research study

You can do so in the following ways:

- By mail:
Study Subject Adviser
Advarra IRB
6940 Columbia Gateway Drive, Suite 110
Columbia, MD 21046
- or call **toll free:** 877-992-4724
- or by **email:** adviser@advarra.com

Please reference the following number when contacting Advarra: Pro00030585.

CONSENT STATEMENTS

PARTICIPANT’S CONSENT (should the participant become cognizant during the study)

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed and dated consent document.

Participant’s Printed Name

Participant’s Signature

____/____/____
Date

STATEMENT OF ASSENT (should the adolescent become cognizant during the study)

I would like to be in this study.

Printed Name of Adolescent Participant

Adolescent Assent Signature

Date

STATEMENT OF PARENTAL / LEGAL GUARDIAN PERMISSION

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree for my child to participate in this study until I decide otherwise. I do not give up any of my or my child’s legal rights by signing this consent document. I will receive a copy of this signed and dated consent document.

Signature of Parent/Legal Guardian (if subject is under age 18) ____/____/____
Date

Printed Name of Parent/Legal Guardian (if subject is under age 18)

INFORMED REFUSAL OF FURTHER PARTICIPATION

You should feel that you have been told enough about this study to give your informed consent before signing this form. Signing this form does not waive any legal rights to which you or the person you represent are entitled. You will receive a copy of this form after it is signed and dated.

If you DO NOT want your family member (or the person you represent) to continue to participate in this study, please sign below.

Participant Name

Printed Name of Legally Authorized Representative (LAR)

Your relationship to act on behalf of Participant (i.e., spouse, child, parent, sibling, other [if other, please describe])

Signature of LAR ___/___/___ ___:___ AM/PM
Date Time

Principal Investigator/Designee Name Title

Designee Signature ___/___/___ ___:___ AM/PM
Date Time