STUDY TITLE: Intraoperative monitoring and management protocol to reduce strokes (IMMPRES): Pilot study

IRB: STUDY20070328

NCT04543838

Informed Consent Document: 06/21/2022

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: **Intraoperative monitoring and management protocol to reduce strokes (IMMPRES): Pilot study**

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- Internal funding, UPMC

KEY INFORMATION

1. As a patient scheduled for cardiac surgery at UPMC, you may be eligible to participate in a research study. A member of the study team will explain the study to you and will answer any questions you might have. Your decision to participate is completely voluntary.

2A. Summary of the research

Purpose of the research: The purpose of this study is to better understand how monitoring the brain and spinal cord during surgery, and using that information to drive blood pressure management, may affect important neurologic and psychiatric outcomes (such as stroke).

Duration, number of study visits: There are five timepoints associated with participation in this study. You will be asked to participate for approximately 3 hours total (6 half-hour sessions over 1 year). This will involve completing surveys and undergoing one Magnetic resonance imaging (MRI) scan. The timepoints will occur at 1) sometime before your surgery, 2) immediately after surgery, 3) after surgery but before discharge from the hospital, 4) 30 days after surgery, 5) 3 months after surgery, and 6) approximately 1 year after surgery.

Overview of study procedures:
At all study timepoints, you will complete questionnaires that assess your physical function, depression, sensory function, cognitive function, and quality of life. You will undergo physical and neurological examination and a post-operative MRI. At the signing of this consent form, you will be randomized into either the intervention or control group like flipping a coin. Those in the intervention group undergo Electroencephalogram (EEG) and somatosensory evoked potentials (SSEP) monitoring during surgery. Those in the control group will receive standard of care during surgery.

3. Reasonable, foreseeable risks or discomforts

Risks of exposure to strong magnetic field & positioning in MRI scanner:

Common Risks: nervousness, unable to tolerate MRI scans due to anxiety, back pain, discomfort due to noise level

4. Reasonable, expected benefits
There will be no direct benefit to you from participating in the study. However, this study will help the researchers learn more about how surgical monitoring factors affect important neuroscience outcomes.

Why is this research being done?
You are being asked to take part in a research study. Research Studies include only people who choose to take part. The study team members will explain the study to you and will answer any questions you might have. You should take your time to make your decision. The purpose of this study is to better understand how surgical monitoring factors affect important neuroscience outcomes. Your doctor may be involved as an investigator in this research study. Before agreeing to participate, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not obligated to be a part of any research study offered by your doctor.

Who is being asked to take part in this research study?
Any adult who is over 18 years of age and is scheduled to have cardiac surgery at UPMC may be able to participate in this study.
We plan to recruit up to 80 people to participate.

What procedures will be performed for research purposes?
There are five timepoints associated with participation in this study. Each timepoint (aside from surgery) will last for approximately a half hour and occur on different day. The timepoints will occur at:
1) Sometime before your surgery
2) Immediately after surgery
3) After surgery but before discharge from the hospital
4) 30 days after surgery
5) 3 months after surgery
6) Approximately 1 year after surgery
The study procedure involves completing questionnaires, and this may take place in any private location. The first timepoint will occur during your visit to the Center for Perioperative Care clinic, your surgeon's office visit, or on admission to the hospital for your surgery. The cognitive assessments Digit Symbol Substitution Test, Trail Making Test part B (TMT-B), and Montreal Cognitive Assessment (MoCA) will be conducted in-person. For post-operative timepoints, subjects will have in-person visits during their hospitalization. The MRI will be obtained prior to discharge from the hospital. The MRI will be completed at the MRI Research Center. The post-operative sessions at thirty days, 3 months, and one year after surgery will be performed in-person. Your medical records will be reviewed for screening and data collection research purposes.

If you decide to take part in this research study, you will undergo the following procedures:

Study Procedures:
If you qualify to take part in this research study, you will undergo the study procedures listed below:

1. Sometime before your surgery, you will be asked by one of your physicians or one of the study investigators to complete several questionnaires. These assessment include the NIH stroke Scale, Questionnaire for Verifying Stroke-Free Status (QVSFS), Delirium Screen, Modified Rankin Scale, Barthel Index, Cognitive Assessment (Digit Symbol Substitution

Test, Trail Making Test part B (TMT-B), and Montreal Cognitive Assessment (MoCA)), Depression Scale, and Quality of Life scale. The assessments will assess physical function, depression, sensory function, cognitive function, and quality of life. Research staff will collect information about your medical history, medications, and may conduct a physical exam. This visit will take approximately a half hour.

During this visit, you will be randomized into one of two groups, like flipping a coin. The first group is the intervention group where you would receive standard medical therapy with monitoring and management. This would include a) intraoperative monitoring with SSEP and EEG during surgery and continued for 4 hours after; b) management protocol will be treating patients based on monitoring results. The second group is the control group where you would receive standard of care intraoperative monitoring. No study procedures will occur to learn what standard of care procedures you will receive, consult with your surgeon. The only difference between these groups occurs during the day of surgery outlined below.

2. During and immediately after surgery, the following research procedures will occur:
   a. If you are assigned to the control group, you will receive standard of care intraoperative monitoring. No study procedures will occur at this time point. There is no time investment for the control group on the day of surgery.
   b. If you are assigned to the intervention group, you will receive intraoperative monitoring with SSEP and EEG during surgery and continued for 4 hours after. This will include electrodes attached via adhesive to your scalp, neck, and shoulders in order to monitor your brain activity after a small electrical current is sent through a probe to the skin near a nerve on your wrist or ankle. An electroencephalogram (EEG) is a test that detects electrical activity in your brain using small, metal discs (electrodes) attached to your scalp. The SSEP test monitors the nerve pathways that are responsible for feeling pressure, touch, temperature and pain. SSEP monitoring assess the signal that is sent to the brain. After the monitoring period, the electrodes will be removed and the study procedures for the day will be over. The research procedures of applying and removing the electrodes will last approximately a half hour.

3. After your surgery before discharge, you will be asked to complete questionnaires to assess your physical function, depression, sensory function, cognitive function, and quality of life. Research staff will collect information about your medical history, medications, and conduct a physical exam. A neurological examination will be performed by study Neurologist 18 to 54 hours after your surgery. This exam includes the NIH stroke Scale, Delirium Screen, Digit Symbol Substitution Test, Trail Making Test part B (TMT-B), and Montreal Cognitive Assessment (MoCA) which assess cognitive and sensory function. An MRI will be performed after your procedure, around the time of discharge from the hospital. These study procedures will take approximately a half hour.

4. Approximately thirty days after surgery, you will be asked to complete questionnaires. These assessments include the Questionnaire for Verifying Stroke-Free Status (QVSFS), Modified Rankin Scale, Barthel Index, Depression Scale, Digit Symbol Substitution Test, Trail Making Test part B (TMT-B), Montreal Cognitive Assessment (MoCA), and Quality of Life scale. The assessments will assess physical function, depression, sensory function, cognitive function, and quality of life. This will be done as a remote telemedicine/Microsoft Teams research visit. This visit will take approximately a half hour. The Microsoft Teams/telemedicine videoconferencing will not be recorded or stored.

5. Approximately three months after surgery, you will be asked to complete questionnaires.

These assessments include the Questionnaire for Verifying Stroke-Free Status (QVSFS), Modified Rankin Scale, Barthel Index, Depression Scale, Digit Symbol Substitution Test, Trail Making Test part B (TMT-B), Montreal Cognitive Assessment (MoCA), and Quality of Life scale. The assessments will assess physical function, depression, sensory function, cognitive function, and quality of life. This will be done as a remote telemedicine/Microsoft Teams research visit. This visit will take approximately a half hour. The Microsoft Teams/telemedicine videoconferencing will not be recorded or stored.

6. Approximately one year after surgery, you will be asked to complete questionnaires. These assessments include the Questionnaire for Verifying Stroke-Free Status (QVSFS), Modified Rankin Scale, Barthel Index, Depression Scale, Digit Symbol Substitution Test, Trail Making Test part B (TMT-B), Montreal Cognitive Assessment (MoCA), and Quality of Life scale. The assessments will assess physical function, depression, sensory function, cognitive function, and quality of life. This will be done as remote telemedicine/Microsoft Teams research visit. This visit will take approximately a half hour. The Microsoft Teams/telemedicine videoconferencing will not be recorded or stored.

Questionnaires: The National Institutes of Health Stroke Scale (NIHSS) was developed to help physicians objectively rate severity of ischemic strokes. The Questionnaire for Verifying Stroke-Free Status (QVSFS) is an 8-item structured interview designed to identify stroke-free individuals. The Modified Rankin Scale (mRS) is used to measure the degree of disability in patients who have had a stroke. The Barthel Index (BI) is a widely used measure of basic activities of daily living function (self-maintenance skills such as dressing, bathing, and grooming). The Montreal Cognitive Assessment (MoCA) is a widely used screening assessment for detecting cognitive impairment. The depression scale PHQ-9 is a multipurpose instrument for screening, diagnosing, monitoring and measuring the severity of depression. The EQ-5D-5L is a self-assessed, health related, quality of life questionnaire. The Trail Making Test is a neuropsychological test of visual attention and task switching. It consists of two parts in which the subject is instructed to connect a set of 25 dots as quickly as possible while still maintaining accuracy. Digit symbol substitution test (DSST) is a test sensitive to brain damage, dementia, age and depression. It consists of digit-symbol pairs followed by a list of digits. Under each digit the subject should write down the corresponding symbol as fast as possible

What are the possible risks, side effects, and discomforts of this research study?
Other aspects of the study involve some risk, which are described below.

Risks of blood pressure (BP) management protocol

Infrequent Risks: Though increasing BP in response to brain activity changes is thought to improve outcomes, there is a small chance that this could cause unforeseen harm. Blood pressure management will be institutional standard of care.

Risks of questionnaires

Infrequent Risks: discomfort with disclosure of personal information
Rare: Breach of confidentiality
If you feel uncomfortable about answering a question, you can choose not to answer it. Research staff will be available to answer any questions you may have about the questionnaires or your responses. There is a potential risk of breach of confidentiality that is standard in all research protocols. There is a possibility that if research data were to become known, this knowledge could potentially impact a subject's future or have a negative impact on family or social relationships.

Risks of MRI scan

Common Risks: nervousness, unable to tolerate MRI scans due to anxiety, back pain, discomfort due to noise level

- You may feel nervous and/or unable to tolerate MRI scans due to anxiety during the MRI scans.
- While the MRI is running, you will be asked to lie still on a narrow bed inside of the scanner and the scanner will make a loud knocking or beeping sound. The noise level is within safety limits, but you will be asked to wear earplugs, since this noise is uncomfortable for some people. You will be in verbal contact with the investigators and operator of the MRI machine, and you can request that the experiment (and scanning) be stopped at any time, and you would be immediately removed from the scanner.
- During the scanning process, you are lying on your back, and it is possible that you may feel some discomfort related to positioning.
- There are no known long-lasting side effects from MRI scanning.

Infrequent Risks: damage to implanted device or tissue injury from migration of embedded metal.
Rare: There are 2 rare risks of having an MRI while you have epicardial pacing leads (metal wires that are often used during cardiac surgeries) retained inside your body. One is that the wires could heat from the interaction with the MRI magnet and cause a burn on your skin. The second is that the wires and magnet could affect the rhythm of your heart and change it in a way that is not normal. We will reduce the risk of this happening by following guidance from the MRI Safety Committee at UPMC for the safest way to do the scan, which includes:
1. Doing a thorough screening for any metal in or on your body prior to the scan, as is done for all MRI
2. Using an MRI machine for this study that has a lower magnet strength that is much less likely to interact with the leads
3. Having you wear a "pulse ox" clip on your fingertip that is safe to wear in the MRI while you are being scanned. The pulse ox can detect any change in your heart rate right away. The MRI technologist will be watching for this and will stop the scan if there is any concern.
4. Having physician investigator readily available to address any issues that may arise.
You may ask the MRI tech to stop the scan if you report a heating sensation or at any time

If your clothing is uncomfortable, or contains metal, you will be asked to change (in a private dressing room) into a hospital gown prior to entering the MRI scanner. You will be prescreened using a standard institutional assessment to determine if it is safe for you to undergo an MRI. This standard safety practice will include questions asked by the investigator about your medical history.

Risks of Electroencephalogram (EEG)

Rare: There is a potential risk of mild irritation from the adhesive used to attach the electrodes to the skin. In rare instances, an EEG can cause seizures in a person with a seizure disorder.

Risks of somatosensory evoked potentials (SSEP)

Rare: There is a potential risk of mild irritation from the adhesive used to attach the electrodes to the skin.

Risks of collection & storage of personal health information

Rare: Breach of confidentiality
There is a potential risk of breach of confidentiality that is standard in all research protocols. There is a possibility that if research data were to become known, this knowledge could potentially impact a subject's future or have a negative impact on family or social relationships.

Although every reasonable effort has been taken, confidentiality during Internet communication activities cannot be guaranteed and it is possible that additional information beyond that collected for research purposes may be captured and used by others not associated with this study.

What are possible benefits from taking part in this study?
You will receive no direct benefit from taking part in this research study.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
Although unlikely, you would be promptly notified if any new information develops during the course of this research study which suggests that you were put at any increased risk as a result of your participation. You will be promptly notified if any new information we learn during this research study may cause you to change your mind about continuing to participate in the study.

Will my insurance provider or I be charged for the costs of any procedures performed as part of this research study?
Neither you, nor your insurance provider, will be charged for the costs of any of the procedures performed for the purpose of this research study. Standard of care procedures will be billed to your insurance.

Will I be paid if I take part in this research study?
You will not be compensated for participation in this research study.

Commercialization statement
Your data from this research study may contribute to a new discovery or treatment. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. You will not retain any property rights, nor will you share in any money that the investigators, the University of Pittsburgh, or their agents may realize.

What information will be collected about me and who will know about my participation in this research study?
We are also requesting your authorization or permission to review your medical record information for the purposes of this study. No research-derived data will be placed into the medical record. Portions of your medical history will also be extracted from the UPMC electronic medical record, to determine what factors influence your neuropsychological testing results, including mental health history and information relative to your surgery, and whether you may be eligible to undergo MRI testing. Your permission to store this information last indefinitely. You may withdraw your authorization to store your private medical information by submitting it in writing with a date to the PI on page 1. You will be withdrawn from the study if you withdraw this authorization.

To protect your privacy, we will ultimately store this collected information separately from personal identifiers such as your name and contact information. Although we will do everything in our power to protect your privacy and the confidentiality of your records, just as with your medical information for health care purposes, we cannot guarantee the confidentiality of your research records. The identifiable link between your personal formation and your data will be stored for a minimum of 7 years after final reporting of study results, and then this link (your personal information) will be

destroyed. All de-identified data from this study will be kept securely for an indefinite period of time. No third party, including relatives, personal physicians, or insurance companies will be granted access to the identifiable information we collect. It is possible that we may share the information from this study, so that it may be combined with other data in larger future studies. However, your information would only be shared with other researchers without any personal identifiers, so no one would be able to learn your identity. For the purpose of monitoring the conduct of this study, authorized UPMC hospitals or other affiliated health care providers from the University of Pittsburgh Office of Research Protections may review your research information.

Is my participation in this research study voluntary?
Yes! Your participation in this research study is completely voluntary. Whether or not you provide your consent for participation in this research study will have no effect on your current or future relationship with the investigators, the University of Pittsburgh, or UPMC. Your participation will not affect your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with any healthcare insurance provider. Your physician is involved as an investigator in this research study. Before agreeing to participate, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your physician.

What happens if I am injured as a result of participation in this research study?
If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation. You waive no legal rights by signing this consent form.

May I withdraw my consent for participation in this research study?
You may withdraw your consent for participation in this research study at any time. Any identifiable research information recorded for, or resulting from, your 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.

To withdraw your consent for participation in this research study, contact the principal investigator of this research study at the address/phone number listed on the first page of this form.

If I agree to take part in this research study, can I be removed from the study without my consent?
You may be removed from the study by the researchers if any practical considerations or safety concerns arise that do not allow you to participate. If the study team loses contact with you during your participation despite reasonable attempts to contact you, you may be withdrawn from the study without your consent.

Will clinically relevant results be available to me?
Though unlikely that any clinically-relevant abnormalities would be detected by these surveys, any such results could be disclosed to you, at the discretion of one of the study physician investigators. A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by US Law. This website will not include information that can
identify you. At most, the website will include a summary of the results. You can search this website at

any time.

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VOLUNTARY CONSENT

The above information has been explained to me and my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions 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, concerns or complaints be addressed by a listed investigator.

I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that have occurred during my participation. By signing this form, I consent to participate in this research study and provide my authorization to share my medical records. A copy of this consent form will be given to me.

_____	_____	_____
Participant's Signature	Printed Name of Participant	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.

I further certify that no research component of this protocol was begun until after this consent form was signed.

_____	_____
Printed Name of Person Obtaining Consent	Role in Research Study

_____	_____
Signature of Person Obtaining Consent	Date