Washington University in St. Louis

INFORMED CONSENT DOCUMENT

Project Title: Ketamine for Postoperative Avoidance of Depressive Symptoms: The K-PASS Feasibility Trial

Principal Investigator: Bradley Fritz, MD

Research Team Contact: Bradley Fritz, MD: bafritz@wustl.edu, (314) 273-3453

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant.

KEY INFORMATION

The first section of this document contains some key points that the research team thought you would find important. The research study is described in more detail after this section.

This is a research study conducted by Dr. Bradley Fritz having to do with the use of low-dose ketamine to prevent patients with a previous history of depression from developing symptoms of depression after surgery. You should carefully consider the information in this consent document and discuss it with the research team. Be sure you understand why you might want to participate, or why you might not want to participate. You may choose to participate or not.

If you agree and sign this consent, you will be volunteering to participate in the research study. All of the information below will be explained and is listed in more detail in the consent document below. The research team must give you a copy of this signed consent document.

How will this study affect me?

- The purpose of this research study is to learn whether it is feasible to conduct a larger, longer trial in the future to learn about the effects of low-dose ketamine on symptoms of depression after surgery.
- As a voluntary participant, you will be asked to spend roughly 15 hours on study activities (mostly while you are already in the hospital for your surgery).
- You were selected because you are scheduled for surgery at Barnes-Jewish Hospital with planned hospital admission and you have a past medical history of depression.
- You will be in this study for approximately one month.
    - There will be one visit before surgery either at the Center for Preoperative Assessment and Planning or in the hospital. This visit will last approximately 1 hour.
    - You will wear a lightweight headband to collect data about your brain wave activity for one night at home before surgery.
    - There will be one visit immediately following your surgery, when the study infusion is

given. There is a 50% chance you will receive ketamine and a 50% chance you will receive saline placebo. This will last approximately 3 hours.
    - There will be approximately 5 follow-up visits after the study infusion is completed. The final visit will be 14 days after you receive the study infusion. If you are discharged from the hospital, these will be telephone visits. Each visit will last approximately 30-40 minutes.
- You will need to come to Barnes-Jewish Hospital, and study visits will occur while you are in the hospital for your surgery. When you are discharged from the hospital, any remaining follow-up will occur by telephone.
- The main risks to you are a possibility of feeling light-headed or unusually happy, having perceptual changes, or having difficulty concentrating while receiving the study infusion. More detail about risks is provided below.
- You will be paid $25 for participating in this study. You will not have costs for participating.
- If you withdraw from the study, the research team may continue to use information already collected about you in this study.

The rest of this document provides more details about the study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you are scheduled for surgery at Barnes-Jewish Hospital with planned intensive care unit admission and you have a past medical history of depression.

The purpose of this research study is to learn whether it is feasible to conduct a larger, longer trial in the future to learn about the effects of low-dose ketamine on symptoms of depression after surgery. Because ketamine may prevent depressive symptoms through changes in brain electrical activity, this study will also determine how brain electrical activity changes during and after the ketamine infusion.

Ketamine is approved by the U.S. Food and Drug Administration to provide anesthesia during surgery and other medical procedures**.** However, the use of ketamine is considered investigational in this study.

In this study, you will randomly be assigned (like flipping a coin) to one of two treatments:
- There is a 50% chance that you will receive a ketamine infusion.
- There is a 50% chance that you will receive a saline placebo infusion. A placebo is a substance that looks like the study drug but contains no active treatment.

WHAT WILL HAPPEN DURING THIS STUDY?

If you agree to participate in this study, we will (1) collect information about your baseline health before surgery, (2) treat you with the randomly-assigned study infusion (either ketamine or placebo) after your surgery, and (3) collect information about your health for up to 14 days after you receive the study medication. These procedures are described in more detail below.

Before Your Surgery

We will collect information about your baseline health either while you are visiting the Center for Preoperative Assessment and Planning or while you are admitted to the hospital (if you are in the hospital before your surgery). We will ask you questions about your medical history, medications, psychiatric history, and mood and emotions. You will also complete a survey about your mood and emotions. You may skip any questions that you prefer not to answer.

The research team will show you how to wear a lightweight headband for the study. This device, the DREEM, is used to assess sleep quality at home. It will allow us to record brain electrical activity from your scalp using electroencephalography, or EEG. EEG is currently used to study brain function in the operating room and for assisting in the diagnosis of sleep problems.

First, we will show you the DREEM and how to wear it. After we show you an instruction card, we will determine the best fit for wearing the device. We will then have you wear the DREEM so that we may obtain baseline data. We will then send you home with the DREEM to wear while you sleep for 1 night before you have surgery. We will call you before and after every day of recording to assist you in this process.

We will ask you to bring the DREEM back on the day of surgery. Alternatively, if you are in the hospital on the night before surgery, we will help you wear it and discuss with your nurses and doctors how it will not impede their care for you.

During your surgery, the research team will not make any changes to the anesthesia that you receive, except that we will ask your anesthesiologist not to give you ketamine during surgery.

After Your Surgery – Day of Study Infusion

At the end of your surgery, the research team will check on you in the operating room. As long as you are not having breathing problems requiring a ventilator, you will receive the study infusion in the recovery room following your surgery. If you are requiring a ventilator, we will delay the study infusion until you are no longer requiring the ventilator. If you are still requiring a ventilator three days after your surgery, then you will no longer be eligible to continue participating in the study.

We will have you wear a DREEM throughout the study infusion. Your nurse will give you either ketamine or placebo through your IV for 3 hours. They will be checking your blood pressure, heart rate, oxygen levels, and other vital signs throughout the infusion. At one time point during the infusion, the research team will ask you questions about how you are feeling and thinking.

If you should experience medication side effects that cause disturbing and/or distressful mental states, your IV infusion medication dose may be decreased to lessen the symptoms. At any time, you or the study doctor may decide to terminate the study and the study infusion will be stopped promptly.

After the Study Infusion

The night following the study infusion, you will wear the DREEM overnight.

The day following the study infusion, the research team will ask you questions about your mood, emotions, and pain. You will also complete a survey about your mood and emotions. You may skip any questions that you prefer not to answer. That evening, you will wear the DREEM overnight again.

The research team will periodically visit you in the hospital to repeat these questions about your mood, emotions, and pain. You will also complete the survey about your mood and emotions at each time point. The final visit will be 14 days after the study infusion. If you are discharged from the hospital less than 14 days after the study infusion, then any remaining visits will be conducted by telephone.

In addition, the research team will access your medical record to collect information about your medical history, surgery, anesthesia, and events that occur while you are in the hospital, such as your vital signs and other medications you receive.

- Identifiers may be removed from your private information including data and used for future research or shared with others. If this occurs, we will not ask you for additional consent.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 32 people will take part in this study conducted by investigators at Washington University.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for approximately one month.

- There will be one visit before surgery either at the CPAP clinic or in the hospital. This visit will last approximately 1 hour.
- You will wear a DREEM headband to collect data about your brain wave activity for one night at home before surgery.
- There will be one visit immediately following your surgery, when the study infusion is given. This will last approximately 3 hours.
- There will be approximately 5 follow-up visits after the study infusion is completed. The final visit will be 14 days after you receive the study infusion. If you are discharged from the hospital, these will be telephone visits. Each visit will last approximately 30-40 minutes.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Risks of KETAMINE

Likely	• Feeling light-headed, "high", exhilarated, and/or happy. • Having perceptual changes or hallucinations, or floating sensations. • Difficulty concentrating, paying attention, or remembering as many items as usual from a list (like items on a grocery list). • Mild and temporary increases in blood pressure.
Less Likely	• Feeling dizzy, sleepy, anxious, suspicious, nauseated.
Rare	• Feeling sad, scared, confused, and/or disoriented. • Moderate and temporary increases in blood pressure. • Future abuse of ketamine. • Prolonged psychosis in individuals with a pre-existing psychiatric condition.

DREEM EEG [Electroencephalography]: Skin irritation may occur from wearing these electrodes. Some discomfort may occur when we change the electrodes, particularly those over your hair.

Questionnaires: You may experience minor discomfort when completing the interviews and assessments. During the interviews in this study, if any particular question makes you uncomfortable, you may discuss its relevance to the study with the specially trained interviewer. You may choose not to answer any question with which you still feel uncomfortable. You can also request to take breaks and continue at another time.

Breach of Confidentiality: One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled "How will you keep my information confidential?" for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?

You may or may not benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because results from this research study will help researchers learn about using ketamine infusions for patients undergoing surgery who have a history of depression.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Instead of being in this study, you could undergo your planned surgery without being in this study.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

As part of this study you will receive tests and procedures that are similar to what you would receive during routine clinical care of your condition. Your health plan/insurance company will be billed for some or all of these costs, and you will be responsible for any co-pays and deductibles that are normally required by your health plan/insurance. Not all insurance plans cover the costs associated with being in a study. Even if they do, you may be responsible for more out-of-pocket expenses, such as co-pays and deductibles, when there are more tests and procedures or more expensive tests and procedures involved in the study than if you were to receive routine clinical care outside the study.

If you wish to know whether there are more tests and procedures or more expensive tests and procedures in the study, you should ask your study doctor.

If you wish to know whether your insurance will pay, you should contact them directly, or speak with the study team about obtaining a financial pre-certification prior to enrolling in the study.

The sponsor is providing the ketamine at no cost to you.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study.

You will be asked to provide your social security number (SSN).You may also need to provide your address if a debit card will be mailed to you.
You will be compensated with a $25 debit card for your study involvement. To receive payment, you must complete the final study visit 14 days following the study infusion.

We will provide you with information about any fees or restrictions on the use of the debit card.

WHO IS FUNDING THIS STUDY?

National Institute of Mental Health (NIMH) is funding this research study. This means that Washington University is receiving payments from NIMH to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from NIMH for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator at 314-273-3453 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by Washington University**.** If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

Other people such as those listed below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- Government representatives (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- National Institute of Mental Health (NIMH)
- Hospital or University representatives to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records and will be available to anyone with access to your health care record, including your health insurance company. This information may also be released as part of a release of information request.
- The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures.
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.
- Any report or article that we write will not include information that can directly identify you. The journals that publish these reports or articles require that we share your information that was collected for this study with others to make sure the results of this study are correct and help develop new ideas for research. Your information will be shared in a way that cannot directly identify you.

To help protect your confidentiality, we will have all paper documents locked in a filing cabinet in a locked office of a member of the study team. We will keep all electronic documents on secured servers that are password protected and have various state of the art firewall protections with frequent upgrades of these protections. Access to these electronic research files will be restricted to members of the research team and will be controlled by the principal investigator.

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.

To further protect your privacy, this research is covered by a Certificate of Confidentiality from the federal government. This means that the researchers can refuse to disclose information that may identify you in any legal or court proceeding or to anyone who is not connected with the research except if:

- there is a law that requires disclosure, such as to report child abuse and neglect, or harm to self or others*;*
- you give permission to disclose your information, including as described in this consent form; or
- it is used for other scientific research allowed by federal law.

This Certificate may not be effective for information held in foreign countries.

You have the right to share your information or involvement in this study with anyone at any time. You may also give the research team permission to disclose your information to a third party or any other person not connected with the research.

If information about you or your involvement in this research is placed in your medical record the information may no longer be protected under the Certificate. However, information in your medical records is protected in other ways.

Are there additional protections for my health information?

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?"

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- your treatment or the care given by your health provider.
- your insurance payment or enrollment in any health plans.
- any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
    - To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ or you may request that the investigator send you a copy of the letter.

- **If you revoke your authorization:**
  - The research team may only use and share information already collected for the study.
  - Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.
  - You will not be allowed to continue to participate in the study.

Can we contact you by email?
We would like to contact you by email for the purposes listed below. Some of these messages may contain health information that identifies you.

- Provide you with a copy of the informed consent
- Send you links to instructional contents
- Send you links to survey questionnaires

Only the research team will have access to your email communications. We will only communicate in this method to send you the information listed above. If you have any questions, wish us to stop sending these messages or need to contact us for an urgent or emergent situation, please contact the research team member identified at the top of this document.

You should be aware that there are risks associated with sending your health information via email.

- There is always a risk that the message could be intercepted or sent to the wrong email address. To avoid this, we will send a test message to ensure we have the correct email address.
- When using any computer you should be careful to protect your username and password. Make sure you log-out before getting up from the computer.
- If you share a home computer or cell phone with other family members, and do not want them to know you are participating in this study make sure you provide an email address that only you can access.
- Your employer will have access to any messages sent or received on any electronic devices used for work or through a work server.
- If you lose your phone, others may be able to access the messages that we send.

Do you agree to allow us to send your health information via email?

_____ Yes **_____ No**
Initials **Initials**

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ under Withdrawing from a Research Study.

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the investigator might decide to end your participation in this research study earlier than planned. This might happen for no reason or because you are found to be ineligible to continue or because in our judgment it would not be safe for you to continue.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Bradley Fritz, MD, at (314) 273-3453. If you experience a research-related injury, please contact: Bradley Fritz, MD, at (314) 273-3453.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office at 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, http://hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 02/14/23.

_____ _____

(Signature of Participant) (Date)

_____

(Participant's name – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that they understand the risks, benefits, and procedures involved with participation in this research study.

_____ _____

(Signature of Person who Obtained Consent) (Date)

_____

(Name of Person who Obtained Consent - printed)