NCT# 04019002

# UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
# CONSENT TO PARTICIPATE IN A RESEARCH STUDY

**Study Title: Evaluating Hyperpolarized and Proton Brain Metabolism in Patients with Glioblastoma.**

STUDY SUMMARY:

Introduction: We are asking you to consider taking part in a research study being done by Susan Chang, M.D., from the University of California, San Francisco (UCSF) Department of Neurosurgery.

The first part of this consent form gives you a summary of the study. We will give you more details about the study later in this form. The study team will also explain the study to you and answer any questions you have.

Research studies include only people who choose to take part. It is your choice whether you want to take part in this study. Please take your time to decide about participating. You can discuss your decision with your family, friends, and health care team.

Researchers want to evaluate the role of novel MR metabolic imaging for assessing patients with glioblastoma. Through this, we hope to improve the way we manage patients in future.

Study Procedures: If you chose to be in this study, you will be receiving novel MR metabolic imaging with standard MR imaging. The research component includes an injection of an investigational agent, called hyperpolarized $^{13}C$ pyruvate, to obtain dynamic metabolic imaging. There are three groups in this study, and depending on which group you are assigned to, you may have one or repeated examinations. Prior to any imaging, you will go through screening procedures to ensure your eligibility.

You will be in this study for a maximum of 4 months. Depending on your study group, you will visit the imaging research site approximately 1 to 3 times.

**Possible Risks:** There are risks to taking part in a research study. Some of the most likely risks of participation in this study include:

- Pain at the injection site
- Bruising at the injection site
- Feelings of claustrophobia while in scanner
- Temporary hearing lost from loud banging noise while in scanner

There are also rare but serious risks of participation, like:

- Allergic/bad reaction to gadolinium

We'll tell you about the other risks later in this consent form.

**Possible Benefits**: There will be no direct benefit to you from participating in this study.

**Your Other Options:** You are free to choose not to participate in the study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

## DETAILED STUDY INFORMATION

This part of the consent form gives you more detailed information about what the study involves.

You are being asked to take part in this study because you have brain cancer.

### WHY IS THIS STUDY BEING DONE?

The purpose of this study is to evaluate whether new metabolic imaging will be useful to physicians and patients with glioblastoma for making treatment decisions and seeing how well various types of treatment work.

The new metabolic imaging will use hyperpolarized $^{13}$C pyruvate, which allows for pictures of the brain that we won't be able to get with standard imaging. Hyperpolarized $^{13}$C pyruvate has not been approved for use by the Food and Drug Administration (FDA) and is available for research only. This investigational agent is a non-radioactive isotope of carbon. The doses of $^{13}$C Pyruvate that will be used in this study have been shown to be safe and well tolerated in a previous human study.

The National Cancer Institute will be providing funding to support the conduct of the research part of the study.

### HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 90 people may participate in the study at UCSF.

### WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

There are three groups in this study. Your study doctor will tell you which group you will be participating in prior to your enrollment. Your assignment to a study group depends on the status of your disease and the type of treatment you will be receiving.

Subjects in Group 1 will have two MR examination time points. Each time point includes a hyperpolarized $^{13}$C pyruvate injection for research imaging as well as standard MRI. The MR examinations will occur before receiving standard of care treatment with radiation and chemotherapy, and at the first post-radiation follow-up scan.

Subjects in Group 2 will have one MR examination time point with hyperpolarized $^{13}$C pyruvate injection for research and standard MRI. This MR examination occurs before surgery.

Subjects in Group 3 will have three MR examinations time points. Each time point includes a hyperpolarized $^{13}$C pyruvate injection for research imaging as well as standard MRI. The MR examinations will occur prior to initiating therapy (baseline), at approximately 7-14 days after initiation of therapy, and 6-8 weeks after the initiation of therapy.

**Before you begin the main part of the study...**

You will need to have the following tests or procedures to find out if you are eligible for the study. These are part of regular clinical care and may be done even if you do not join the study. You will also have some procedures that are only being done because you are in the study. These are called study procedures and are noted as "study test" in the list of procedures below. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

You must complete your Screening procedures within 14 days prior to participating in the study. Your screening visit may take up to 2 hours depending on which procedures you have.

- A **medical history**: this will include questions about your health, current medications including natural or herbal products, demographic data, and prior medical history including information about your brain cancer.
- A **physical exam**: This examination will be similar to those done for your regular medical care, and will also include measurements of blood pressure, heart rate, respiratory rate, body temperature, and how much oxygen in your blood.
- **Karnofsky Performance status**: This is an assessment tool to measure your ability to perform everyday tasks.
- **Blood drawing (venipuncture)**: You may be asked to give a blood sample for laboratory tests. Less than 2 teaspoons of blood will be drawn by inserting a needle into a vein in your arm. Blood (approximately 1-2 teaspoons) will be drawn through a vein in your arm for routine safety tests.

**During the main part of the study...**

If the exams, tests and procedures show that you can be in the main part of the study, and you choose to take part, then you will need the following tests and procedures. Your MR exam will be performed at the UCSF Department of Radiology Imaging Center located at the Mission Bay campus [redacted]. Your visit including the MR exam will take less than 2 hours.

***The following procedures are for all patients.***

<u>At Baseline before the Pyruvate Injection:</u>

- Vital signs - blood pressure, heart rate, respiratory rate, body temperature, and how much oxygen in your blood
- Your IV/injection site will be monitored
- You will be placed in the MR scanner and anatomic images will be acquired to define the most appropriate location for obtaining the $^{1}H$ metabolic data
- The Pyruvate will be placed in a syringe and brought into the scan room

Following approval by the study pharmacist, you will receive the Pyruvate into a vein over a period of less than one minute. Shortly after the injection has started, you will be imaged for $^{13}C$ metabolic imaging, which will be obtained for a period of 2-3 minutes. Afterwards, a second set of anatomic images may be acquired immediately afterwards. During this time, you will be observed for side effects.

<u>At approximately 10 minutes after Pyruvate injection</u>

- The MR scanner table will be pulled out and the set-up modified to obtain standard MR data
- You will be asked if you are experiencing any side effects
- Your injection site will be monitored

You will then continue receiving the MR exam with the imaging data similar to those used for clinical purposes. You may receive an injection of Gadolinium if it has been requested by your oncologist for diagnostic purposes, which won't require a second IV placed.

If you are in Group 1 or 3, you will have repeated MR imaging examinations. Subjects in Group 1 will receive two MR examinations, at the time before receiving standard of care treatment with radiation and chemotherapy, and at the first post-radiation follow up scan (8 weeks later). Subjects in Group 3 will undergo three research imaging examinations, prior to initiating therapy (baseline), at approximately 7-14 days after the initiation of therapy, and 6-8 weeks after the initiation of therapy. Subjects in group 1 or 3 are required to undergo repeat screening to verify that you still meet eligibility criteria. This will include repeat assessment of Karnofsky performance status, vital signs, physical examination, medication history in addition to monitoring for adverse events and evaluation of the prior injection site. You will then undergo imaging (with associated procedures and monitoring) as per the first imaging examination. Patients in Group 2 will receive one MR imaging examination before surgery.

**Study location:** All imaging study procedures will be done at the UCSF Mission Bay campus.

## HOW LONG WILL I BE IN THE STUDY?

Patients enrolled in Group 3 will participate in the study for a maximum of 4 months, due to having three research imaging examinations over time.

## CAN I STOP BEING IN THE STUDY?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop so that they can make arrangements for you to do so.

It is important to tell the study doctor if you are thinking about stopping so that any risks from the pyruvate can be checked. Another reason to tell your doctor that you are thinking about stopping is to talk about what follow-up care and testing could be most helpful for your cancer treatment.

The study doctor may stop you from taking part in this study at any time if they believe it is in your best interest, if you do not follow the study rules, or if the study is stopped.

## WHAT SIDE EFFECTS OR RISKS CAN I EXPECT FROM BEING IN THE STUDY?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your healthcare team may give you medicines to help lessen side effects. Many side effects go away soon after the pyruvate is completed. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

You should talk to your study doctor about any side effects that you experience while taking part in the study.

### *Risks and side effects related to Hyperpolarized Pyruvate ($^{13}C$) Injection*

**Likely**

- Bruising at the injection site
- Pain at the injection site

**Less Likely**

- Fatigue
- Dizziness
- Decreased sensitivity to touch
- Increased heart rate
- Low blood pressure

- Headache
- Feeling hot/flushing
- Taste disturbance
- Smell disturbance
- Dry mouth
- Urgency to use the bathroom
- Throat pain

***Risks related to Study Procedures***

**Blood Drawing (venipuncture) risks:** Drawing blood may cause temporary discomfort from the needle stick, bruising, and infection.

ECG risks: Risks associated with ECG are redness or swelling where the patches are applied on your body.

**MRI scan risks:** Because the MRI machine acts like a large magnet, it could move iron-containing objects in the MRI room during your examination, which in the process could possibly harm you. Precautions have been taken to prevent such an event from happening; loose metal objects, like pocket knives or key chains, are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker, you will not be allowed into the MRI room and cannot have an MRI.

Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia and by the loud banging noise during the study. Temporary hearing loss has been reported from this loud noise. This is why you will be asked to wear ear plugs. At times during the test, you may be asked to not swallow for a while, which can be uncomfortable.

For your MRI scan, you will lie down on a narrow bed, which will then be placed in a tunnel, which is 6 feet long by 2 feet wide. We may ask you to be repositioned for the acquisition of imaging data after the pyruvate injection. The MRI scan takes approximately an hour and a half to complete.

**Contrast agent (gadolinium) risks**: A few side effects of gadolinium injection such as mild headache, nausea, and local pain may occur. Rarely (less than 1% of the time) low blood pressure and lightheadedness occurs. This can be treated immediately with intravenous fluids. Very rarely (less than one in one thousand), patients are allergic to gadolinium. These effects are most commonly hives and itchy eyes, but more severe reactions have been seen which result in shortness of breath.

Patients with severe kidney disease sometimes have a bad reaction to gadolinium contrast agents. The condition is called nephrogenic systemic fibrosis (NSF). It can cause skin to tighten or scar and can damage internal organs. Sometimes it can be life threatening. There are no reports of NSF in patients with normal kidney function. Before you have a MRI scan requiring an injection of gadolinium contrast, you will have a blood test in order to check the function of your kidneys. Based on your medical history and the results of the test, a doctor will decide whether it is safe for you to undergo the MRI scans. Gadolinium can build up in the brain. UCSF prefers to use gadobutrol, which is less likely to build up in the brain, compared to other types of gadolinium. However, for some types of liver imaging, a less stable agent called gadoxetate is sometimes required.

Gadolinium as an MRI imaging agent will only be used when medically necessary for your care. When it is medically necessary, the study doctors believe that the clear benefits of using gadolinium for imaging outweigh the unknown risks, which is minimized by using gadobutrol.

**Reproductive risks:** You should not father a baby or become pregnant while on this study because the drugs in this study can affect an unborn baby. It is important to understand that you need to use birth

control while on this study. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study.

**Unknown Risks:** The pyruvate injections may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

For more information about risks and side effects, ask your study doctor.

## ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

There will be no direct benefit to you from participating in this study. However, this study will help doctors learn more about and gather more information about magnetic resonance (MR) imaging to develop future clinical trials, and it is hoped that this information will help in the treatment of future patients with brain cancer.

## WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

You are free to choose not to participate in the study. If you decide not to take part in this study, there will be no penalty to you. You will not lose any of your regular benefits, and you can still get your care from our institution the way you usually do.

Your physician will discuss these other options with you. Please talk to your doctor about your choices before deciding if you will take part in this study.

## WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?

We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Cancer Institute (NCI) and other government agencies, e.g., the Food and Drug Administration (FDA), involved in overseeing research
- UCSF Helen Diller Family Comprehensive Cancer Center
- The University of California
- Governmental agencies in other countries where the Pyruvate agent may be considered for approval.

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible. A medical record will be created because of your participation in this study. Your consent form and some of your research test results will be included in this record. Therefore, your other doctors may become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

## ARE THERE ANY COSTS TO ME FOR TAKING PART IN THIS STUDY?

The study will provide pyruvate and administration of pyruvate at no cost to you. Two types of procedures will be done during this study. Some are part of your standard medical care and others are only for research. You or your insurer will be billed for the standard medical care. You will be responsible for your co-pays, deductibles, and any other charges that your insurer will not pay. There is a possibility that your insurer may not cover all standard medical care costs, if you are receiving medical services out of network. Any procedures done only for research will not be charged to you or your insurer.

## WILL I BE PAID FOR TAKING PART IN THIS STUDY?

You will not be paid for taking part in this study.

In return for your time and travel expenses, your parking will be covered for taking part in this study.

## WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

It is important that you tell your study doctor Susan Chang, MD if you feel that you have been injured because of taking part in this study. You can tell her in person [redacted].

**Treatment and Compensation for Injury:** If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs or covered by the University of California depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415- 476-1814.

## WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you, and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

## WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact your study doctor Susan Chang, MD [redacted].

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the Office of the Institutional Review Board at 415-476-1814

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.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call **1-800-4-CANCER (1-800-422-6237)** and ask them to send you a free copy.

## CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health

information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

_____
Printed Name of Participant

_____ _____
Date Participant's Signature for Consent

_____
Printed Name of Person Obtaining Consent

_____ _____
Date Person Obtaining Consent

_____ _____
Date Witness-Only (required if the participant is a non-English Speaker)