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

Study Title: Hyperpolarized 13C pyruvate metabolic MRI to predict renal tumor aggressiveness

Research Project Director:	Zhen Jane Wang, M.D., Professor of Radiology. UCSF, [redacted], San Francisco, CA. Phone: [redacted]; Email: [redacted]

Study Coordinator:	Calista Chiu, Clinical Research Coordinator Phone: [redacted]; Email: [redacted]

This is a clinical research study. Your study doctor, Zhen Jane Wang, MD and her associates from the University of California San Francisco (UCSF) Department of Radiology, and UCSF Department of Urology will explain the study to you.

Research studies include only people who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because you have a kidney tumor.

Why is this study being done?

The purpose of this study is to investigate if a newly developed imaging technique called hyperpolarized 13C magnetic resonance imaging (MRI) can help doctors determine noninvasively whether a kidney tumor is a benign tumor or cancer, and if cancer, how aggressive it is. This will help doctors and patients in the future to make better treatment decisions. During your MRI scan, you will be injected with an investigational agent called 13C pyruvate alone or in combination with 13C, 15N urea, a similar investigational agent, in order for doctors to better study the kidney tumor you have on MRI.

Hyperpolarized 13C pyruvate and 13C, 15N urea are investigational imaging agents. An investigational agent is one that has not been approved for clinical use by the Food and Drug Administration (FDA) and is available for research only. The dose of 13C pyruvate and/or 13C, 15N urea that will be used in this study has been shown to be safe and well-tolerated in multiple previous human studies. To perform this imaging, the investigational imaging agent is injected into a vein and then an MRI scan is performed.

The National Institute of Health and the American Cancer Society will be providing funding for this study.

How many people will take part in this study?

Up to 100 people will take part in this study.

What will happen if I take part in this research study?

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

You will need to have the following exams, tests or procedures to find out if you can be in the main part of the study. These should be completed within 28 days before you receive the MRI scan. Many of these exams, tests or procedures are part of regular clinical care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- Physical examination - This will include a complete medical history, vital signs (e.g. blood pressure, heart rate, temperature), height and weight.
- A review of medications you are taking (including over-the-counter medications and supplements)
- MRI safety screening: we will ask you a series of questions to make sure it is safe for you to have an MRI exam.

All women who are capable of becoming pregnant will be asked to undergo a urine pregnancy test on the day of the scan, and if they're pregnant, they will not be able to participate in the study.

During the main part of the study...

If the above 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 MRI exam will be performed at the UCSF Department of Radiology Imaging Center located at the Mission Bay Campus in Byers Hall.

- You will have your vital signs (e.g. blood pressure, heart rate) checked prior to entering the MRI scanner.
- You will undergo an abbreviated MRI exam to obtain imaging data similar to those used for clinical purposes. You will lie down on a narrow bed, which will then be placed in a tunnel that is 6 feet long by 2 feet wide and open at each end for your MRI exam. You will lie there quietly in the MRI scanner for between 45-90 minutes. You will be monitored while you are in the MRI scanner. You may receive an injection of Gadolinium contrast agent for your MRI if it has been requested by your clinical doctor for diagnostic purposes. Gadolinium contrast agent is approved for clinical use, and helps make the tumor more visible in images.
- You will then receive 13C pyruvate injection into an arm vein over a period of less than one minute. Shortly after the injection has started, MRI data will be obtained for a period of 2-3 minutes. During this time, you will be observed for side effects.

- (**OPTIONAL**) You will be asked if you would like to receive an optional, second injection of 13C pyruvate or an optional second injection of combined 13C pyruvate and 13C, 15N urea followed by a repeat MRI. This can be done either within 15-30 minutes following the first hyperpolarized 13C MRI scan, or you can return within 1-2 weeks and receive the second optional hyperpolarized 13C MRI. You will only receive the second hyperpolarized 13C MRI scan if you do not experience any side effects from the first injection. The second hyperpolarized 13C MRI is not required to participate in this study. These are used to provide additional information on the tumor. You will be asked whether you would like to receive the optional second hyperpolarized 13C MRI at the end of this consent form.
- (**OPTIONAL**) If you and your doctor decide that you will undergo active surveillance of your tumor (active surveillance means to monitor the tumor closely using clinical CT or MRI scans, instead of immediate surgery), you will be asked if you would like to undergo optional repeat hyperpolarized 13C pyruvate MRI, usually around the same time as the clinical CT or MRI scans for active surveillance. You may optionally receive 2 additional hyperpolarized 13C MRI scans during the active surveillance.
- Your vital signs will be measured again once you are off the MRI scanner.
- In addition, we will make sure you are not experiencing any side effects. If you experience any side effects deemed clinically significant by the monitoring MD or nurse on site, you will be monitored closely until stable, and an MD or nurse will follow up with you with a phone call within 24 hours to assess for other side effects.

If your urologist has determined that, as part of your standard-of-care, you will have an operation to remove your kidney tumor, and if you agree, the study doctors will collect left over tissue from the operation to correlate tissues changes with changes seen from the MRI exam. This is discussed in the About Using Tissue for Research section of this consent form.

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

How long will I be in the study?

The screening procedures to determine whether you can participate in the main part of the study will take up to 1 hours. For the main part of the study, your visit for the MRI exam will take up to 2 hours. If you decide to proceed with an optional second hyperpolarized 13C MRI scan during the same visit, the visit will take up to 3 hours. If you decide to proceed with an optional second hyperpolarized 13C MRI scan on a separate visit, within 1-2 weeks from the first hyperpolarized 13C MRI scan, the second visit will take up to 2 hours. If you and your doctor decide that you will undergo active surveillance of your tumor, you may optionally receive 2 additional hyperpolarized 13C MRI scans during the active surveillance period, with each MRI scan take up to 2 hours.

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. He or she will tell you how to stop your participation safely.

Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes 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 health care team may give you medicines to help lessen side effects. Many side effects go away soon after 13C pyruvate injection is completed. In some cases, side effects can be serious, long lasting, or may never go away. There is also a risk of death.

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

Risks and side-effects related to 13C pyruvate or combined 13C pyruvate and 13C, 15N urea injections:

Common (>10% of people)

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

Rare (occurring in less than 1% of people)

- 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:

- **Placement of Venous catheter:** The placement of a venous catheter may cause temporary discomfort from the needle stick, bruising, infection, and fainting.

- **MRI 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 earplugs. At times during the MRI, you may be asked to not swallow for a while, which can be uncomfortable.

- **Reproductive risks:** Because the risks to a fetus from 13C pyruvate are unknown, pregnant women must not participate in this study. Women should not breastfeed a baby while participating in this study.

- **Incidental findings:** It is possible that doctors may notice incidental findings on your MRI that could be important to your health. In the event that your scans reveal any potential health concerns, your images may be referred to a qualified UCSF clinician. If it is discovered that you have any incidental findings that require follow-up, the study doctor or a member of the UCSF clinical staff may contact you. If you have doctor at UCSF who referred you to be in this study, we may also convey the incidental findings to that doctor so he or she may help you choose the best follow-up.

- **Unknown Risks:** The experimental treatments 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 methods of 13C pyruvate MRI to noninvasively determine how aggressive a kidney tumor is and to develop future clinical trials using this method. It is hoped that this information will help in the treatment of future patients with kidney tumors.

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 to not 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.

How will information about me be kept confidential?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Some information from your medical records will be collected and used for this study. If you do not have a UCSF medical record, one will be created for you. Your signed consent form and some of your research tests will be added to your UCSF medical record. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your medical record as a result of your participation. Study tests that are performed by research labs, and information gathered directly from you by the researchers will be part of your research records, but will not be added to your medical record. 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.

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- Representatives of the University of California
- Representatives of the National Institute of Health, and American Cancer Society
- Other government agencies, e.g., the Food and Drug Administration (FDA), involved in overseeing research

Are there any costs to me for taking part in this study?

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. The sponsor will provide 13C pyruvate and MRI scans following injection of 13C pyruvate at no cost to you.

Will I be paid for taking part in this study?

You will be paid $75 for undergoing each 13C pyruvate injection followed by a MRI scan. If you choose to take part in the optional second injection of 13C pyruvate or optional second injection of combined 13C pyruvate and 13C, 15N urea followed by a MRI scan, you will be paid a total of $150.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, Zhen Jane Wang, MD, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her [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 and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board 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 Zhen Jane Wang, MD [redacted].

A description of this clinical trial is 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.

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.

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OPTIONAL RESEARCH

Please note: This section of the informed consent form is about optional research studies that are being done with people who are taking part in the main study. You may take part in these optional studies if you want to. You can still be a part of the main study even if you say "no" to taking part in any of these optional studies.

You can say "yes" or "no" to each of the following studies. Please mark your choice. for each study.

Optional second injection of 13C pyruvate or optional second injection of combined 13C pyruvate and 13C, 15N urea followed by a MRI scan

The study doctor would like your permission to perform an optional second injection of 13C pyruvate or optional second injection of combined 13C pyruvate and 13C, 15N urea followed by a MRI scan. This can be done either within 15 to 30 minutes following completion of the first scan, or on a separate visit within 1-2 weeks from the first scan. The purpose of the second scan is to see if it will provide additional information on your kidney tumor metabolism. Since kidney tumor metabolism is affected by perfusion, the purpose of a co-polarized pyruvate and urea injection is to provide information on perfusion and enable correction for its effects.

Benefits
There will be no direct benefit to you for receiving a second injection of 13C pyruvate or optional second injection of combined 13C pyruvate and 13C, 15N urea followed by a MRI scan. Information from this scan will be used to see if it provides additional information on your kidney tumor metabolism.

Risks
There are currently several studies across the country using multiple 13C pyruvate injection as well as injection of combined 13C pyruvate and 13C, 15N urea. To date, patients in those studies have not experienced any adverse side effects.

Things to Think About

The choice to have a second 13C pyruvate injection or second injection of combined 13C pyruvate and 13C, 15N urea followed by a MRI is up to you. No matter what you decide to do, it will not affect your care. The risks to you would be same as the main part of the study. If you have any questions, please consult your study doctor.

Please read the sentence below and think about your choice. After reading the sentence, put your initials in the "Yes" or "No" box. If you have any questions, please talk to your doctor, or call our research review board at IRB's phone number.

No matter what you decide to do, it will not affect your care.

1. I agree to receive a second 13C pyruvate injection or optional second injection of combined 13C pyruvate and 13C, 15N urea followed by a MRI 15-30 minutes following the first scan or on a separate visit within 1-2 weeks following the first scan.

YES	NO

<u>Repeat hyperpolarized 13C pyruvate and optional combined 13C pyruvate and</u> 13C, 15N urea <u>MRIs while you are on active surveillance</u>

If you and your doctor decide that you will undergo active surveillance of your tumor, the study doctor would like your permission to perform up to 2 additional hyperpolarized 13C pyruvate and optional combined 13C pyruvate and 13C, 15N urea MRI scans during the active surveillance period.

Benefits
There will be no direct benefit to you for receiving additional hyperpolarized 13C pyruvate and optional combined 13C pyruvate and 13C, 15N urea MRIs. Information from these will be used to see if the metabolism of your kidney tumor changes over time and whether this is related to any kidney tumor growth.

Risks
There are currently several studies across the country using multiple 13C pyruvate injection as well as injection of combined 13C pyruvate and 13C, 15N urea and MRI scans. To date, patients in those studies have not experienced any adverse side effects.

Things to Think About

The choice to have additional hyperpolarized 13C MRI scans is up to you. No matter what you decide to do, it will not affect your care. The risks to you would be same as the main part of the study. If you have any questions, please consult your study doctor.

Please read the sentence below and think about your choice. After reading the sentence, put your initials in the "Yes" or "No" box. If you have any questions, please talk to your doctor, or call our research review board at IRB's phone number.

No matter what you decide to do, it will not affect your care.

1. I agree to receive up to 2 additional hyperpolarized 13C pyruvate and optional combined 13C pyruvate and 13C, 15N urea MRIs during the active surveillance period.

YES	NO

Using Tissue for Research

If your urologist has determined that, as part of your standard-of-care, you will have an operation to remove your kidney tumor, and if you agree, the study doctors will collect left over tissue from the operation. The tissue will be kept at UCSF, and used to correlate tissues changes with changes seen on the MRI exam.

The research that may be done with your tissue is not designed to specifically help you. It might help people with kidney tumors in the future. If the results from this analysis are published, your data will not be reported individually. Results from this analysis will not be given to you or your

clinical doctor. These results will not be put in your health record. The research will not affect your care.

Things to Think About
The choice to let us keep the leftover tissue for future research is up to you. No matter what you decide to do, it will not affect your care.
If you decide now that your tissue can be kept for research, you can change your mind at any time. Just contact the study doctor, Zhen Jane Wang, MD (address below), and let us know that you do not want us to use your tissue. Then any tissue that remains will no longer be used for research.

Zhen Jane Wang, MD
Department of Radiology and Biomedical Imaging
University of California San Francisco
[redacted]
San Francisco, CA 94143
[redacted]

In the future, people who do research may need to know more about your health. While the study doctor may give them reports about your health, it will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Your tissue will be used only for research and will not be sold.

Benefits
The benefits of research using tissues in this study include learning more about the MRI findings by correlating to tissues changes.

Risks
The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small. To further safeguard your privacy, information obtained as part of this study will not be placed in your medical record.

Making Your Choice
Please read the sentence below and think about your choice. After reading the sentence, put your initials in the "Yes" or "No" box. If you have any questions, please talk to your study doctor, or call our research review board at IRB's phone number.

No matter what you decide to do, it will not affect your care.

1. My leftover tissue from kidney tumor operation may be kept to study how tissue findings are associated with findings on MRI scans.

YES	*NO*

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.

_____ _____
Date Participant's Signature for Consent

_____ _____
Date Person Obtaining Consent

_____ _____
Date Witness – Only required if the participant is a non-English speaker