Consent Form

Title of Research Study: ***Radioembolization (RE) of Primary and Secondary Liver Malignancies and the Effect on the Immune System: A Prospective Study of Cytokine Modulation and Immune Cell Infiltration***

Investigator Team Contact Information: ***Shamar Young, MD***

For questions about research appointments, the research study, research results, or other concerns, call the study team at:

Investigator Name: Shamar Young, MD Investigator Departmental Affiliation: Radiology Phone Number: 612-626-5388 Email Address: youn1862@umn.edu	Study Staff Phone Number: 612-624-6904

Supported By: This research is supported by departmental resources within the Department of Radiology at the University of Minnesota.

Key Information About This Research Study

The following is a short summary to help you decide whether or not to be a part of this research study. More detailed information is listed later on in this form.

What is research?

Doctors and investigators are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to learn new things in order to help groups of people in the future. Investigators learn things by following the same plan with a number of participants, so they do not usually make changes to the plan for individual research participants. You, as an individual, may or may not be helped by volunteering for a research study.
- The goal of clinical care is to help you get better or to improve your quality of life. Doctors can make changes to your clinical care plan as needed.

Your doctor, who is also responsible for this research study, is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Why am I being asked to take part in this research study?

We are asking you to take part in this research study because you have been diagnosed with liver cancer and will be receiving radioembolization (RE) therapy to treat this particular type of cancer.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide

Why is this research being done?

The importance of creating an immune system response when treating cancer has been researched extensively over the last several decades. There has been research looking into immune response after other similar treatment methods such as external beam radiation and thermal ablation. However, there is not much known regarding how the immune system responds after radioembolization (RE) treatment. The goal of this study is to investigate how your body's immune system responds after treating your liver cancer with RE. Participation in this study will not provide any direct benefit to you, but will provide vital information that could improve treatment options for other liver cancer patients in the future.

How long will the research last?

We expect that you will be in this research study for 12 weeks after you receive RE of the liver.

What will I need to do to participate?

You will be asked to undergo screening to assess your eligibility for the study and sign consent documents. Any additional laboratory tests or biopsies that need to be completed to assess eligibility will be ordered. After you receive RE of the liver, we will ask you to attend 4 visits at 1 week, 2 weeks (optional), 4 weeks, and 12 weeks post treatment. At visit weeks 1, 4, and 12, your blood will be drawn for laboratory analysis. The week 2 visit includes an optional CT- or ultrasound-guided liver biopsy. If you choose not to have the second biopsy, you will not need to attend the week 2 visit.

More detailed information about the study procedures can be found under ***"What happens if I say yes, I want to be in this research?"***

Is there any way that being in this study could be bad for me?

As part of this study you will undergo either an ultrasound or CT scan to conduct the two liver biopsy procedures (one biopsy before RE, and the second biopsy 2 weeks after RE). The initial biopsy may be part of your standard medical care. If it is not done as part of your standard medical care, it will be conducted for study purposes. The second biopsy is optional and for research only. The decision to utilize ultrasound or CT depends on the doctor's assessment of your health and the best method to guide the liver biopsy. CT scans involve exposure to ionizing radiation. If you have CT-guided biopsies done for research, the radiation exposure is not necessary for your medical care and is for research purposes only. The average amount of radiation that the average person would receive from these scans is approximately 7.3 times that received from natural sources of radiation by a Minnesota resident in one year (3 mSv). This exposure involves minimal risk and is necessary to obtain the research information desired. Ultrasounds are widely considered to be a safe procedure in which low-power sound waves are used.

Risks of hepatic tumor biopsy include significant bleeding, which can require blood transfusion or a secondary procedure, infection, tumor cells transferring outside the liver capsule due to puncture, or accidental damage to surrounding structures. The procedure may also cause some pain and discomfort. In very rare cases, people might have an allergic reaction to the numbing medicine. The allergic reaction could include rash/hive, flushing of the face, itching, wheezing and tightness in the throat. There will be a small scar from the biopsy.

The risks of taking blood include pain, a bruise at the point where the blood is taken, redness and swelling of the vein and infection, and a rare risk of fainting.

If you have participated in any other study within the past 12 months you may not be eligible to participate in this study. It is your responsibility to inform the investigator of such involvement prior to the beginning of the proposed study.

Will being in this study help me in any way?

There are no benefits to you from taking part in this research. However, the information obtained from this study could benefit liver cancer patients in the future.

Detailed Information About This Research Study

The following is more detailed information about this study in addition to the information listed above.

How many people will be studied?

We expect about 30 people will be in this research study.

What happens if I say "*Yes, I want to be in this research*"?

You will be scheduled for a consultation visit to discuss your RE treatment plan. At this visit we will review your current laboratory results and order any additional laboratory tests that would be required to determine your eligibility. Please see the table below titled "Screening Procedures" for a further description of the timeline.

If you are eligible, we will ask you to come back prior to treatment to have a CT- or ultrasound-guided biopsy of your liver. This biopsy may be part of your standard medical care. If it is not done as part of your standard medical care, it will be conducted for study purposes. You will also have blood drawn to assess your immune markers for research (approximately 3 tablespoons of blood).

The RE treatment is part of your standard medical care. After you receive treatment, you will have blood drawn again at 1, 4, and 12 weeks post-treatment for research (approximately 3 tablespoons of blood each time). An optional, second CT- or ultrasound-guided needle biopsy will be conducted for research purposes at two weeks post treatment. If your biopsy is CT-guided, the procedure will involve you laying in a CT scanner, similar to ones you may have been in before, and CT being used to guide a small needle into your tumor. If your biopsy is ultrasound-guided, you will be lying down so the doctor can use the ultrasound to guide the needle into the liver. Regardless of the method used, tissue samples will then be collected. You will receive medications to keep you comfortable during this process. Please see the table below titled "Study Timeline" for a further description of the tests and timeline. Your blood draws will occur during your standard of care clinic visits whenever possible and those will all happen at the University of Minnesota Medical Center or the Clinics and Surgery Center. The liver biopsies will be conducted at the University of Minnesota Medical Center-Fairview East Bank Hospital. This is an outpatient procedure and you can expect to be discharged the same day.

Screening Procedures:

	Screening	
	within 28 days of enrollment	within 14 days of enrollment
Written Consent	R	
Medical history	S	
Confirmation of hepatic metastases meeting study eligibility requirements	R	
Provider assessment for eligibility	R	
ECOG performance status	R	
Complete Blood Count with diff (CBC), international normalized ratio (INR)		S
Total bilirubin		S
Pregnancy test (urine or serum) WOCBP[1]		S[1]

[1]For women of childbearing potential (WOCBP): urine pregnancy test within 14 days prior to study registration. If a urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required.
R = Research; S = Standard medical care

Study Timeline:

	Prior to RE	**Treatment**	**Time post RE**			
			1 week (± 6 days)	2 weeks (±7 days) ***optional***	4 weeks (± 2 weeks)	12 weeks (± 2 weeks)
Assess for adverse events		R	R	R	R	R
Blood draw for labs: cytokines and lymphocytes	R		R		R	R
Tumor biopsy	S or R			R		
Radioembolization treatment		S				

R = Research; S = Standard medical care

If you agree, the investigator may retain any leftover blood or tissue samples taken during the study. This is optional. These samples may be used for other research not related to this study. These samples will be labeled with a unique code, and samples can only be linked back to you by using the master list. Only the study team will have access to the master list. A link must be maintained so that information gained from the samples can be compared to information gathered in other aspects of the trial. We will store these samples for up to 15 years after completion of the study for future analysis. However, if you agree to storage now and later change your mind, you may request to have any remaining identifiable samples destroyed by contacting the study doctor or another member of the study staff.

What are my responsibilities if I take part in this research?
To attend the post-radioembolization clinic visits as scheduled and provide the needed blood and tissue samples as detailed above.

What happens if I say "Yes", but I change my mind later?
You can leave the research study at any time without impacting your usual standard clinical care

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. This means that your choice not to be in this study will not negatively affect your right to any present or future medical care.

We will obtain all data that has been collected, up until the point of you notifying study personnel you no longer wish to participate but will no longer access you or your medical records further.

What do I need to know about reproductive health and/or sexual activity if I am in this study?
You should not be or become pregnant while in this research study.

If you are sexually active, both men and women should use at least one effective means of birth control while participating in this research study. According to the World Health Organization and the United States Center for Disease Control and Prevention, the most effective forms of birth control include complete abstinence, surgical sterilization (both male and female), intrauterine devices (IUDs), and the contraceptive implant. The next most effective forms of birth control include injectables, oral contraceptive pills, the contraceptive ring, or the contraceptive patch. Acceptable, but least effective, methods of birth control include male condoms (with or without spermicide) and female condoms.

Will it cost me anything to participate in this research study?
Taking part in this research study will not lead to any costs to you.

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay. In some cases, insurance will not pay for services ordinarily covered because these services are performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

What happens to the information collected for the research?
Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the Institutional Review Board (IRB), the committee that provides ethical and regulatory oversight of research, and other representatives of this institution, including those that have responsibilities for monitoring or ensuring compliance, such as the Masonic Cancer Center and Fairview Health Services.

Data or Specimens Collected
When identifiers are removed from your private information or samples that are collected during this

research, that de-identified information or those samples could be used for future research studies or distributed to another investigator for future research studies without your additional consent.

Most tests done on samples in research studies are only for research and have no clear meaning for health care. The investigators will not contact you or share your individual test results.

The monitors, auditors, the IRB, the University of Minnesota Research Compliance Office and other University compliance units, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), the US Food and Drug Administration (FDA) may be granted temporary direct access to your medical records to conduct and oversee the research. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available at 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.

Will anyone besides the study team be at my consent meeting?

You may be asked by the study team for your permission for an auditor to observe your consent meeting. Observing the consent meeting is one way that the University of Minnesota makes sure that your rights as a research participant are protected. The auditor is there to observe the consent meeting, which will be carried out by the people on the study team. The auditor will not document any personal (e.g. name, date of birth) or confidential information about you. The auditor will not observe your consent meeting without your permission ahead of time.

Whom do I contact if I have questions, concerns or feedback about my experience?

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 or go to https://research.umn.edu/units/hrpp/research-participants/questions-concerns. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact

information and “Whom do I contact if I have questions, concerns or feedback about my experience?” of this form for HRPP contact information.

Can I be removed from the research?

The person in charge of the research study can remove you from the research study without your approval. Possible reasons for removal include failure to comply with the study protocol and inability to obtain adequate liver biopsies or blood samples.

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury let the study physicians know right away.

Will I be compensated for my participation?

If you agree to take part in this research study, we will pay you up to $75 for your time and effort. You will be given $25 for attending follow-up visits for blood draws at 1 week, 4 weeks, and 12 weeks after treatment (a total of $75 if you attend all three). These follow-up visits may not line up with your standard of care medical appointments, so we will compensate you for the additional time and travel.

Payment will be made using a pre-paid debit card called Greenphire ClinCard. It works like a bank debit card. We will give you a debit card and each time you receive a payment for participation in this study, the money will be added to the card after each completed visit.

You may use this card at any store that accepts MasterCard or you can use a bank machine to remove cash. However, there may be fees drawn against the balance of the card for cash withdrawals (ATM use) and inactivity (no use for 3 months). We will give you the ClinCard Frequently Asked Questions information sheet that answers common questions about the debit card. You will also receive letters with additional information on how you can use this card and who to call if you have any questions. Be sure to read these letters, including the cardholder agreement, for details about fees.

The debit card system is administered by an outside company. The company, Greenphire, will be given your name. They will use this information only as part of the payment system. Your information will not be used for any other purposes and will not be given or sold to any other company. Greenphire will not receive any information about your health status or the study in which you are participating.

Use of Identifiable Health Information

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Those persons who get your health information may not be required by Federal privacy laws (such as the 1099 Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission. Please read the HIPAA Authorization form that we have provided and discussed.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Optional Elements:

The following research activities are optional, meaning that you do not have to agree to them in order to participate in the research study. Please indicate your willingness to participate in these optional activities by placing your initials next to each activity.

Yes, I agree (initial)	**No, I disagree (initial)**	
_____	_____	The investigator may retain any leftover blood or tissue samples taken during the study. These samples may be used for other research not related to this study.
_____	_____	The investigator may conduct the second CT- or ultrasound-guided biopsy for research purposes two weeks after treatment.

Your signature documents your permission to take part in this research. You will be provided a copy of this document.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent

WITNESS STATEMENT:
The participant was unable to read or sign this consent form because of the following reason:

☐ The participant is non-English speaking

☐ The participant is visually impaired

☐ The participant is physically unable to sign the consent form. Please describe:

_____

☐ Other *(please specify)*:

_____

For the Consent of Non-English Speaking Participants when an Interpreter is Used:
As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

_____ _____
Signature of Interpreter Date

_____
Printed Name of Interpreter

OR:

Statement from a Non-Interpreter:
As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

_____ _____
Signature of Individual Date

_____
Printed Name of Individual