A Pilot Study to Assess Theragnostically Planned Liver Radiation with Functional DVH Analysis to Optimize Individualized Radiation Therapy

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INFORMED CONSENT STATEMENT FOR RESEARCH

A Pilot Study to Assess Theragnostically Planned Liver Radiation with Functional DVH Analysis to Optimize Individualized Radiation Therapy

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ABOUT THIS RESEARCH

You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

TAKING PART IN THIS STUDY IS VOLUNTARY

You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled, and will not affect your relationship with the Roudebush VAMC.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to compare treatment plans that are designed for your radiation treatment. One treatment plan will be created using routine procedures normally performed for radiation treatment planning. The other treatment plan will be created using routine procedures along with additional imaging scans. The study team would like to see if adding these imaging scans to treatment planning can help your doctors administer less radiation to your healthy liver tissue.

You were selected as a possible participant because of your diagnosis of liver cancer.

The study is being conducted by Dr. Ronald Shapiro. It is funded by The Department of Radiation Oncology of the IU School of Medicine.

HOW MANY PEOPLE WILL TAKE PART?

If you agree to participate, you will be one of 20 participants taking part in this research.

WHAT WILL HAPPEN DURING THE STUDY?

If you agree to be in the study, you will do the following things:

Baseline Visit

If you sign this informed consent form, tests or procedures will be done to find out if you can be in the study. These tests may be performed at one or two office visits before any other procedures for this study are performed. Many of these tests may be performed as standard of care for you cancer diagnosis and/or treatment and will not be repeated if not deemed necessary by the study physician.

Simulation Period Visit
If your study doctor decides you can be in the study, prior to receiving any radiation, you will participate in a CT planning and simulation (practice) session that will be used to design your actual treatments. These procedures are done to help doctors gather information about your tumor and liver in order to create a plan for your radiation treatment.

SBRT (stereotactic body radiation therapy)
After the simulation planning session, you will return to the radiation oncology clinic for a total of three to five radiation treatments. Each of the radiation treatments will be separated by several (2 to 8) days. Each treatment will last about an hour and will be performed while you lie in the stereotactic body frame. The frame will help the radiation beams target the site of your cancer. You will have a special type of CT done on the treatment machine and a blood draw before each radiation treatment. You will have additional blood draws performed once you are midway through your radiation treatments. During your treatment you will also be asked questions about how you are feeling, any health problems, your activity and well-being.

End of Treatment Visit
You will return for a follow-up visit approximately 30 days from your last radiation treatment. You will be asked questions about how you are feeling, any health problems, your activity level and general well-being.

Follow Up
You will have additional follow up visits approximately 3, 6 and 12 months after the end of treatment. You will be asked questions about how you are feeling, any health problems, your activity level and general well-being.

Below is listed of all study procedure and their timeframes, that will performed during your participation in the study.

	Baseline	**Post-Consult**	**Mid way through RT**	**End of treatment visit**	**Follow up**
	-4 weeks of Registration	After consult and prior to treatment	Fraction 2 or 3	30 ± 7 days post last treatment	3, 6, and 12-month post-RT
Informed Consent	X				
History	X				
Physical	X				X
Vitals (ht, wt, bp)	X				X
Clinical Assessment			X		
ECOG score	X				X
CBC w/ diff, platelets, CMP, INR	X		X	X	X
AFP or CEA as indicated	X				X
Urine pregnancy test	X				
CTP, MELD, and ALBI scores	X		X		
CT Simulation Scan		X			
MRI with Eovist of abdomen and/or Triple Phase ABD CTG		X			X
HIDA scan		X			X

The procedures below are part of routine standard clinical care.

- Medical History: You will be asked questions about your medical history, demographics and about medications. The study team will review your medical record to obtain information about your medical history.

- Physical exam: A physical exam will be performed by your treating physician or the study doctor.

- Urine pregnancy test: A urine pregnancy test will be performed in women who are able to become pregnant. Approximately 5 mL (1 teaspoon) of urine will be collected.

- Vital Signs will be observed, including your weight, height and blood pressure.

- ECOG performance status will be evaluated, which tells us how well you are able to perform your activities of daily living.

- Blood draw: You will have a blood draw as part of routine care to obtain the following laboratory tests:
    - Complete Blood Count - *this test measures the levels of white blood cells, hemoglobin and platelets in your blood*
    - Complete Metabolic Profile - *this test measures how your kidneys and liver are functioning*
    - AFP/CEA - *this is a tumor marker test that is used to help track liver cancer and response to treatment*
    - INR – *this test measures how quickly your blood clots*

- Child-Turcotte-Pugh (CTP) MELD (Model for End-State Liver Disease) and ALBI (albumin-bilirubin)scores: Your doctor will calculate your CTP and ALBI scores. These scores provides information on how well your liver is working. Your doctor will also calculate your MELD score, which will estimate your life expectancy.

- Triple Phase CT Simulation Scan (abdomen and pelvis): A CT scan is a medical imaging technique that generates a 3-D image of your liver and other organs in the abdomen. This procedure is standard of care for all patients who are planning to undergo SBRT.

WHAT ARE THE RISKS OF TAKING PART IN THE STUDY?

While participating in the study, the risks, side effects, and/or discomforts include:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, and some may never go away.

SBRT Risks

Early side effects

- Fatigue
- Skin reaction (redness/dryness)
- Decreased white blood cell count
- Loss of appetite
- Diarrhea
- Nausea and/or vomiting
- Abdominal pain
- Heartburn
- Worsening of liver function tests, which may be temporary or permanent

Late side effects (rare and tend to occur months or years after treatment)

- Liver damage/liver failure
- Chest wall pain
- Osteoporosis/Increased risk of broken bones (ribs)
- Ulcer or perforation (hole) in the wall of the stomach or small intestine
- Gastrointestinal bleeding

- Bowel obstruction
- Kidney damage
- Secondary cancer
- Spinal cord damage

Risks of Radiation Exposure

Your participation in this research study involves exposure to radiation in addition to what you may receive as part of your standard care due to the addition of the HIDA scan before and after radiation treatment. The radiation dose you are exposed to during treatment will not be increased the benefit from the radiation you receive for your standard care. This outweighs the risk because it allows your doctor to provide appropriate medical care; however, the additional radiation "dose" you receive for research purposes may not benefit you personally. Regulatory agencies have established annual radiation dose limits for both individuals who work with radiation (e.g. x-ray technologists, radiologists, etc.) and those participating in research studies. The additional radiation dose you will receive from participating in this study is less than either of those limits.

Radiation has been shown to cause cancer and/or leukemia from doses that are significantly higher than the additional annual radiation dose you will receive by participating in this study. According to the Health Physics Society (an international organization that specializes in radiation protection), the increased risk of health effects (i.e. cancer and/or leukemia) from radiation doses of this amount is either too small to be observed or nonexistent in a normal population. While there is no evidence that any risk exists for humans exposed to such low levels, it is assumed that the risks rise with lifetime accumulated dose from all sources of ionizing radiation, including the doses you receive from medical procedures and the environment. You should also be aware that everyone's sensitivity to radiation is not the same and some diseases (e.g. genetic diseases, diseases affecting DNA repair, and immune diseases such as HIV) may make you more sensitive to the effects and consequences of the radiation exposure than the normal population. Finally, you should know that even if there is an increased risk of an effect, it could be 5 to 20 years before any effect would actually occur. Thus, you may want to factor in your age, overall health, and the number of medical radiation procedures that you've had when determining if this risk is acceptable to you. The calculated effective dose resulting from your participation in this study is available upon request.

HIDA Scan Risks

The risks involved in a HIDA scan are minimal. They include the following:

- Radiation exposure; a very small amount of radioactive material is used and the radiation exposure is well below the level that causes adverse effects.
- Allergic reactions to the radioactive material; however, this is extremely rare and without documented cases.
- Discomfort, bruising or rash at the injection site or discomfort while lying on the table for the required amount of time for the scan

MRI Risks

MRI scans have very few physical risks or side effects. The contrast agent, Eovist, can cause side effects of headache, nausea, abnormal taste, and feeling hot.

CT Scan Risks

There is a slight risk of developing an allergic reaction to the iodine contrast material. The reaction can be mild (itching, rash) or severe (difficulty breathing or sudden shock). Death resulting from an allergic reaction is rare. The contrast material used during CT scanning can cause water loss or damage to the kidneys that may lead to kidney failure. This is a concern if dehydrated or have poor kidney function. If contrast material is used, diabetics may be at risk for kidney problems, especially if on metformin. There is always a slight risk of damage from being exposed to any radiation, including the low levels of X-rays used for a CT scan. However, the risk of damage from the X-rays is usually very low compared with the potential benefits of the test.

Blood Draw Risks
The needle sticks used to take blood samples may cause discomfort, local pain, bruising, swelling, lightheadedness, dizziness and rarely, fainting and/or a possible infection from the needle stick at the site where the skin is punctured by the needle.
There also may be other side effects that we cannot predict.

WHAT ARE THE POTENTIAL BENEFITS OF TAKING PART IN THE STUDY?
We don't expect you to receive any benefit from taking part in this study, but we hope to learn things which will help scientists in the future.

WHAT ARE THE OTHER TREATMENT OPTIONS?
Instead of being in the study, you may participate in another research study for liver cancer. You can undergo standard radiation treatment planning without being in a study.

WILL I RECEIVE MY RESULTS?
We may learn things about you from the study activities which could be important to your health or to your treatment. If this happens, this information will be provided to you. Your clinician will share these results with you during a clinic visit. You may need to meet with professionals with expertise to help you learn more about your research results. The study team/study will not cover the costs of any follow-up consultations or actions.

HOW WILL MY INFORMATION BE PROTECTED?
Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. No information which could identify you will be shared in publications about this study. VA data will be stored in the IU Clinical Trials database: OnCore system for 8 years after the end of the study.

Research records will be maintained by the investigator in accordance with the VHA Records Control Schedule.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the investigator and his/her research associates, the study sponsor, the Indiana University Institutional Review Board or its designees, the VA Research and Development Committee's designees, and federal agencies, including but not limited to the Office for Human Research Protections (OHRP), the Office of Research Oversight (ORO), VA Office of the Inspector General (OIG), and The Food and Drug Administration (FDA).

A description of this clinical trial will be available on **ClinicalTrials.gov**, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

WILL MY INFORMATION BE USED FOR RESEARCH IN THE FUTURE?
Information collected from you for this study may be used for future research studies or shared with other researchers for future research. If this happens, information which could identify you will be removed before any information is shared. Since identifying information will be removed, we will not ask for your additional consent.

WILL I BE PAID FOR PARTICIPATION?
You will not receive payment for taking part in this study

WILL IT COST ME ANYTHING TO PARTICIPATE?
There will be no costs to you for any of the treatment or testing done as part of this research study. Eligibility for medical care at a VA Medical Center is based upon the usual VA eligibility policy and is not guaranteed by participation in a research study.

You will not be required to pay for medical care or services received as a subject in a VA research project except as follows:

Some veterans are required to pay co-payments for medical care and services provided by the VA. These co-payment requirements will continue to apply to medical care and services provided by VA that are **not** part of this study.

WHO WILL PAY FOR MY TREATMENT IF I AM INJURED?
The VA medical facilities shall provide necessary medical treatment to a research subject injured as a result of participation in a research project approved by a VA Research and Development Committee and conducted under the supervision of one or more VA employees in accordance with applicable federal regulations. This does not apply to (1) treatment for injuries due to noncompliance by a subject with study procedures; or (2) research conducted for VA under a contract with an individual or a non-VA institution.

Financial compensation for research-related injuries is not available. However, by signing this form, you do not give up your legal rights to seek such compensation through the courts.

RESEARCH SUBJECT'S RIGHTS:
Participation in this study is entirely voluntary. You may refuse to participate. Refusal to participate will involve no penalty or loss of rights to which individuals are entitled. You may withdraw from this study at any time without penalty or loss of VA or other benefits. You will receive a copy of this signed consent form.

In case there are medical problems or questions, Dr. Ron Shapiro can be called at 317 988-3652 during the day and Dr. David Long at 317 312-0248 after hours. If any medical problems occur in connection with this study, the VA will provide emergency care.

Please direct questions about the consent process and the rights of research subjects to the VA Customer Service Office at (317) 988-2602. For questions about your rights as a research subject or complaints about a research study, contact the Indiana University Human Subjects Office at 317-278-3458 or 800-696-2949. If you have any questions about the research study or want to check the validity, discuss problems, concerns or obtain information or offer input, please call the VA Research Personnel Office at 317-988-3032.

The study has been explained to me and all of my questions have been answered. The risks or discomforts and possible benefits of the study have been described. Other choices of available treatment have been explained.

PARTICIPANT'S CONSENT

In consideration of all of the above, I give my consent to participate in this research study. I will be given a copy of this informed consent document to keep for my records. I agree to take part in this study.

Participant's Printed Name:_____

Participant's Signature:_____ **Date**:_____

Printed Name of Person Obtaining Consent:_____

Signature of Person Obtaining Consent:_____ **Date**:_____