20-006433

Early Detection, Accurate Staging, and Biologic Characterization of HCC with Hybrid ^{68}Ga-PSMA-Dual -Contrast PET/MRI Using Cyclotron-Produced ^{68}Ga

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MAYO CLINIC

Name and Clinic Number

Approval Date: **October 2, 2024**
Not to be used after: **October 1, 2025**

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: Early Detection, Accurate Staging, and Biologic Characterization of HCC with Hybrid ^{68}Ga-PSMA-Dual -Contrast PET/MRI Using Cyclotron-Produced ^{68}Ga

IRB#: 20-006433

Principal Investigator: Dr. Ajit Goenka and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this research is to know whether 68Ga-PSMA PET/MRI or PET/CT can improve upon the diagnosis and management of hepatocellular carcinoma. You are being asked to take part in this research study because you were recently diagnosed with hepatocellular carcinoma (HCC) and may be a candidate for a liver transplant or may undergo hepatic surgical resection, or locoregional therapy (LRT) (ablation or embolization).
What's Involved	This research study will take you two or three visits to complete. The number of visits depends on your planned procedure that may be taken as part of your standard clinical care. Research procedures may include a up to two PET/CT or PET/MRI scans.

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Key Information	*PET/MR or PET/CT scan using ^{68}Ga-PSMA* The effect of ^{68}Ga-PSMA on a fetus (developing baby still in the womb), or on a breastfeeding infant is unknown and may be harmful. Because of these risks, women cannot take part in this study if they are pregnant or breastfeeding. If you are a female, you must have a negative urine pregnancy test within 48 hours prior to your scan in order to participate in this study unless you cannot become pregnant. As with any medication, allergic reactions are a possibility. The risk of an allergic reaction to ^{68}Ga-PSMA is minimal. As with any new or investigational drug, there may be adverse events or side effects that are currently unknown and it is possible that certain unknown risks could be permanent, serious, or life-threatening. This study is only being done to gather information. You may choose not to take part in this study. This study will not make your health better; it is being done to gather information. We anticipate this information gained from this study will help others with Hepatocellular Carcinoma in the future. You won't need to pay for tests and procedures which are done just for this research study.
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

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Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** Dr. Ajit Goenka **Phone:** (507) 284-4399 **Study Team Contact:** Paula Vo Study Coordinator **Phone:** (507) 293-3885 Maggie Olson Study Coordinator **Phone:** (507) 266-7337 Casey McAdam Study Coordinator **Phone:** (507) 293-0505 **Institution Name and Address:** Mayo Clinic 200 First Street, SW Rochester, MN 55905
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Participant Advocate (RPA)** **(The RPA is independent of the Study Team)** **Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

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Other Information:
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.

Why are you being asked to take part in this research study?

You are being asked to take part in this research study because you were recently diagnosed with hepatocellular carcinoma (HCC) and may be a candidate for a liver transplant or may undergo hepatic surgical resection, or locoregional therapy (LRT) (ablation or embolization).

Why is this research study being done?

The purpose of this research is to know whether ^{68}Ga-PSMA PET/MRI or PET/CT can improve upon the diagnosis and management of hepatocellular carcinoma.

MRI stands for Magnetic Resonance Imaging, a scan that uses magnetic and radio waves to produce detailed structural information of the organs, tissues and structures within the body. PET stands for Positron Emission Tomography, an imaging test that helps to measure the information about functions of tissues and organs within the body. A PET scan uses a radioactive drug (tracer) to show this activity. CT scan uses X-rays to create images of the bones and internal organs within your body.

Combining a PET scan with an MRI or CT scan can help make the images easier to interpret. PET/MRI and PET/CT scans are hybrid scanners that combine both of the two modalities into a single scan. This allows images of both anatomy (MRI or CT) and function (PET) to be taken during the same examination.

The ^{68}Ga-PSMA PET/MRI scan is done with a very small amount of a radioactive tracer called ^{68}Gallium-PSMA. In patients that have been diagnosed with HCC, a protein called prostate-specific membrane antigen (PSMA) appears in large amounts on the surface of the cancerous cells. The PSMA protein was first discovered in human prostate cancer cell lines; however, recent studies have shown that PSMA can also be found on cells of HCC. The healthy cells of the liver do not express the PSMA protein on their surface as much as these cancerous cells.

The radioactive chemical compound (^{68}Ga-PSMA) has been designed to circulate through the body and attach itself to the PSMA protein on HCC cells. A PET/MRI or PET/CT scan is then used to detect the location of HCC lesions. The purpose of this study is to know whether ^{68}Ga-PSMA PET/MRI or PET/CT can improve upon the diagnosis and management of hepatocellular carcinoma in the future.

Information you should know

Who is Funding the Study?
The Department of Defense (DoD), Office of the Congressionally Directed Medical Research Programs (CDMRP), and Mayo Clinic is funding or supporting the study.

Information Regarding Conflict of Interest:
Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation. If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study.

How long will you be in this research study?

This research study will take two to three visits to complete. The number of visits depends on your planned procedure that may be taken for your standard clinical care.

Surgical Resection

If you will potentially undergo a surgical resection as part of your standard of care, you will have two study visits, including a screening visit and one imaging visit. These visits can be done on the same day.

The first visit will be a screening visit in which the study team will review if you are eligible to participate in the research, review the consent form with you, and answer any relevant questions.
If you choose to sign the consent form, your study coordinator will schedule a second visit in which you will undergo a PET/MRI or PET/CT scan within four weeks of recruitment. The PET/MRI or PET/CT visit will be approximately three hours.

Locoregional Therapy (Ablation or Embolization)

If you will potentially undergo Locoregional Therapy (LRT) as part of your standard of care, you will have up to three study visits, including a screening visit and two imaging visits.

During the screening visit, the study team will determine if you are eligible to participate in the research, review the consent form with you, and answer any relevant questions. If you choose to sign the consent form, your study coordinator will schedule the following research procedures on your behalf:

1. A PET/MRI or PET/CT within four weeks of recruitment. A PET/MRI or PET/CT visit will take approximately three hours. You do not have to fast for this appointment.
2. A second PET/MRI or PET/CT scan three months after your standard of care Hepatic Locoregional Therapy (LRT). A PET/MRI or PET/CT visit will take approximately three hours. You do not have to fast for this appointment.

What will happen to you while you are in this research study?

Visit one: Eligibility review and consent

A member of the study team will meet with you to review if you are eligible to participate in the research, review the consent form, and answer any relevant questions. If you choose to sign the consent form, your study coordinator will schedule all research related procedures on your behalf.

Visit two: Imaging appointment

The second visit will consist of either a ^{68}Ga-PSMA PET/MRI scan or a ^{68}Ga- PSMA PET/CT scan.

In women with childbearing potential, a negative urine pregnancy test is required within 48 hours before the administration of radiopharmaceutical.

All study subjects will primarily be assigned to undergo a PET/MRI scan. In the event that you cannot have a PET/MRI scan, a PET/CT scan is available. You will not have both scans.

Details of the PET/MRI or PET/CT scans are as described below:

*If you are having a ^{68}Ga-PSMA **PET/MRI** Scan:*

The PET/MRI scan will be done on the first floor of the Charlton North Building within six weeks of enrollment. This visit will last approximately three hours, including a 30 minute nursing assessment, 90 minutes for ^{68}Ga-PSMA uptake, and 60 minutes for the PET/MRI scan. You do not have to fast for this appointment.

After you check in, a technologist will instruct you to change into a gown and will assess you to ensure that you do not have any metallic devices or implants in your body and, if applicable, perform a pregnancy test. Once the technologist confirms that you are eligible to participate, you will be led into an uptake room in which an intravenous catheter (IV) will be placed in a vein in your arm. This catheter will be used to inject ^{68}Ga-PSMA, a radioactive tracer designed to attach itself to the PSMA protein on HCC cells. After the radioactive tracer is injected, you will be asked to sit and relax quietly for approximately 90 minutes to allow the drug to circulate your body.

Next, a technologist will lead you to the PET/MRI scanner. You will be positioned on the scanner bed on your back with your hands by your sides. The technologist will then begin the 60-minute PET/MRI scan. During this time, it is important to stay as still as possible. A few moments after the scan has started, two gadolinium-based MRI contrast agents, namely, gadoxetate and gadavist will be injected through your IV catheter. Both of these contrast agents are FDA-approved and are extensively used in clinical practice. However, their combined use in this study is considered as investigational. Gadolinium is used to enhance MRI images and provides a better picture of the body. During your scan, it is important to stay as still as possible.

This scan will complete the second study visit. No additional precautions would need to be taken after your scan. If you experience any discomfort or change in your health in the next 48 hours after your scan, please contact the study team.

*If you are having a ^{68}Ga-PSMA **PET/CT** Scan:*

The PET/CT scan will be done on the sixth floor of the Charlton Building within six weeks of enrollment. This appointment will last approximately three hours, including a 30 minute nursing assessment, 90 minutes for ^{68}Ga-PSMA uptake, and 30 minutes for the PET/CT scan. You do not have fast for this appointment.

After you check in, a technologist will assess you and, if applicable, perform a pregnancy test. You will be led to an uptake room in which an intravenous catheter (IV) will be placed in a vein in your arm. This catheter will be used to inject ^{68}Ga-PSMA, a radioactive tracer designed to specifically attach itself to the PSMA protein on HCC cells.

After the radioactive tracer is injected, you will be asked to sit and relax quietly for approximately 90 minutes to allow the drug to circulate your body.

Next, a technologist will lead you to the PET/CT scanner. You will be positioned on the scanner bed on your back with your hands by your sides. The technologist will then begin the 30-minute PET/CT scan. During this scan, it is important to stay as still as possible.

This scan will complete the second study visit. No additional precautions would need to be taken after your scan. If you experience any discomfort or change in your health in the next 48 hours after your scan, please contact the study team.

After the first PET/MRI or PET/CT scan, you will continue with your standard care hepatocellular carcinoma management as advised by your clinical physician.

PSMA Immunohistochemistry Tissue Testing

A part of this research study will also include analysis of tissue samples that have been gathered in your standard of care clinical procedures. Immunohistochemistry (IHC) analysis is a method for demonstrating the presence and location of specific proteins in tissue sections.
Unless you give your permission below, your information or samples collected as part of your standard of care will not be used for analysis in this research study. Please read the following statement below and mark your choice:

I permit my information and samples to be studied as part of this Hepatocellular Carcinoma research study at Mayo Clinic:

☐ Yes ☐ No Please initial here: _____Date: _____

Visit three: Three-month follow-up imaging appointment
*(For participants undergoing **Locoregional Therapy** only)*

Three months after your locoregional therapy (ablation or embolization), you will have the second PET/MRI or PET/CT scan. You will be in the same scanner modality, i.e. PET/MRI or PET/CT, as you had in visit two. Please refer to visit two for additional details of your imaging visit.
Tests done only for research purposes are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your information and samples will not be provided to you.

In the rare event that a finding might affect the health of you or your family, we will contact you and you can choose whether to receive or refuse the information. If you decide to follow up and further medical testing or care is needed, the costs will be billed to you or your insurance.

What are the possible risks or discomforts from being in this research study?

If you take part in this research, you will receive medical imaging studies or procedures that involve exposure to radiation. The amount of radiation from these studies has a low risk of harmful effects.

MRI technologies up to 3.0T and CT technologies have been used in clinical procedures for over 30 years and have a well-documented safety record. Similarly, PET scanners are widely used in clinical practice. The PET/MR and PET/CT scanner do not involve any risks other than those normally associated with routine clinical PET, MRI or CT scans, similar to those already performed in many hospitals.

MRI scan
By using a very powerful magnet, an MR can find things in the body with great accuracy. However, because of the magnet, it's very important that it not be used on patients who have certain types of metal objects in their bodies. The force of the magnet could move these objects within the body and cause serious injury.
Metal can be inside a person's body for several reasons: Implanted medical devices such as a pacemaker, injuries such as bullet fragments, and occupational hazards such as metal shavings from a grinding machine.

You need to tell your doctor or MR technician if you have any metal objects or foreign materials inside you. Even if you only suspect that you might and/or you're not sure where they are, further testing can be done to rule out the possibility.

Possible Discomfort/Hearing Damage from Noise
The MR machine makes loud knocking sounds when it is scanning. Because of this you may be asked to wear earplugs while having your MR scan. The earplugs minimize discomfort from noise and keep the MR noise within the safety range for hearing.

Reactions to Contrast Material (gadoxetate and gadavist)
The MR dye (FDA-approved gadolinium) may cause headache, discomfort at the injection site, nausea or vomiting, tingling, dizziness, and/or warmth at the injection site. Approximately two percent (1 out of 50 patients) experience some side effects. However, these are mostly mild such as nausea and headache. Similar to most medications, gadolinium may cause allergic reactions. In rare cases (1 out of 10,000 patients) the allergic reaction can be life-threatening, if untreated. The radiologist and radiology nursing staffs are trained to treat such allergic reactions, should they arise. Gadolinium should be given with caution in patients with a history of seizures, severe kidney disease, asthma, or hemolytic anemia.

If you have any of these conditions, please tell your doctor so that you can discuss whether you can safely participate in this study. Studies have shown that small amounts of gadolinium may remain in the body of patients who have received these injections. The effect of this, if anything, is unknown at this time.

Exposure to gadolinium contrast material in patients with poorly functioning kidneys may result in a rare but serious and potentially fatal condition known as nephrogenic systemic fibrosis (NSF). This progressive disorder can lead to thick, coarse, or hard skin that severely restricts movement of the joints. If you are known to have kidney disease or poor renal function, you may not be able to take part in this part of the study. The investigator may also ask you to give a blood sample to test your creatinine level; this level is used to measure how well your kidneys are working. If your creatinine level is high, you may not be able to take part in this study.

Intravenous (IV) Line Placement
Intravenous line placement is associated with discomfort and a small risk of bruising or infection at the IV site. To minimize this risk, IV lines will be placed by experienced radiology nurses and technologists who place IV lines.

Possible Claustrophobia (Fear of Small Spaces)
Some people with claustrophobia and others may feel too closed in and may not be able to tolerate MR or CT scanning. If you feel too confined in the MR scanner, you can ask that the scan be stopped after you enter the MR scanner.

PET/MRI or PET/CT scan using ^{68}Ga-PSMA
The effect of ^{68}Ga-PSMA on a fetus (developing baby still in the womb), or on a breastfeeding infant is unknown and may be harmful. Because of these risks, women cannot take part in this study if they are pregnant or breastfeeding. If you are a female, you must have a negative urine pregnancy test within 48 hours prior to your scan in order to participate in this study unless you cannot become pregnant.

As with any medication, allergic reactions are a possibility. The risk of an allergic reaction to ^{68}Ga-PSMA is minimal. As with any new or investigational drug, there may be adverse events or side effects that are currently unknown and it is possible that certain unknown risks could be permanent, serious, or life-threatening.

Sedation
Sedation may be offered to relax you during the scan if you are uncomfortable in small spaces. In order to receive sedation, you must have an adult accompany you to your appointment. You may feel drowsy after you receive sedation and you should not drive, operate machinery or sign legal documents within 24 hours of receiving sedation.

Confidentiality Risk
As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

Are there reasons you might leave this research study early?

You may decide to stop at any time. You should tell the Principal Investigator if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the Principal Investigator or Mayo Clinic may stop you from taking part in this study at any time:

- If it is in your best interest,
- If you don't follow the study procedures,
- If the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?
Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. Treatment costs for research-related injuries not covered by your insurance will be paid by Mayo Clinic.

What are the possible benefits from being in this research study?

This study will not make your health better; it is being done to gather information. We anticipate this information gained from this study will help others with Hepatocellular Carcinoma in the future.

What alternative do you have if you choose not to participate in this research study?

This study is only being done to gather information. You may choose not to take part in this study.

What tests or procedures will you need to pay for if you take part in this research study?

You won't need to pay for tests and procedures which are done just for this research study.

These tests and procedures are:

- PET/MRI or PET/CT Scan(s) with contrast agents
- Urine Pregnancy Test (if applicable)
- ^{68}Ga-PSMA tracer production
- Immunohistochemical evaluation of tissue samples with PSMA antibody

However, you and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care, including co-payments and deductibles.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

You won't be paid for taking part in this study.

Will your information or samples be used for future research?

Identifiable information such as your name, Mayo Clinic number, or date of birth may be removed from your information or samples collected in this study, allowing the information or samples to be used for future research or shared with other researchers without your additional informed consent.

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. All your study information will be coded and stored on a secured password protected server accessible only to study personnel.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so.
Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

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Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- Other Mayo Clinic staff involved in your clinical care.
- The sponsor(s) of this study and the people or groups hired by the sponsor(s) to help perform this research.
- The confidentiality section allows the DoD access to research records as a part of its human subjects protection oversight activities.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- A group that oversees the data (study information) and safety of this research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media) information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private, and it may no longer be protected by the Privacy Rule.

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
Plummer Building PL 3-02
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts forever.

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Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature