^{68}Ga-RM2 PET/MRI for Detection of Regional Nodal and Distant Metastases in Patients with Intermediate and High-Risk Prostate Cancer

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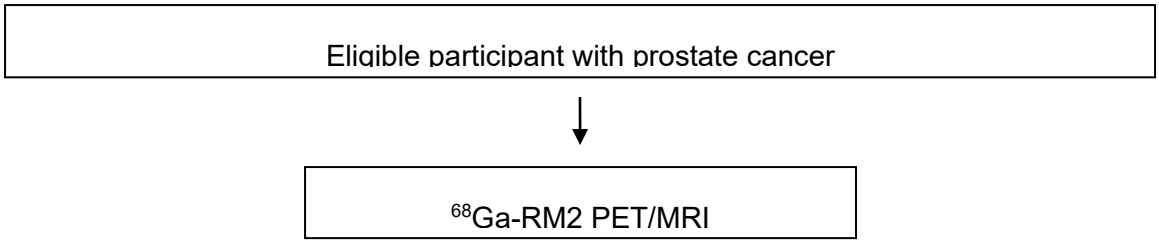
PROTOCOL SYNOPSIS

TITLE	^{68}Ga-RM2 PET/MRI for Detection of Regional Nodal and Distant Metastases in Patients with Intermediate and High-Risk Prostate Cancer
STUDY PHASE	Phase 2
INDICATION	Prostate cancer
INVESTIGATIONAL PRODUCT OR PROCEDURE	^{68}Ga-RM2
PRIMARY OBJECTIVE(S)	To evaluate ^{68}Ga-RM2 PET/MRI for detection of regional nodal and distant metastases in patients with intermediate and high-risk prostate cancer scheduled to undergo prostatectomy with lymph node dissection.
SAMPLE SIZE	90 participants
GOALS	To allow the referring physicians in the GU Oncology group to provide their patients a specific molecular imaging test for prostate cancer that is currently used outside of the United States. To refine the PET/MRI protocols in the setting of initial staging of patients with intermediate and high risk prostate cancers.

SCHEMA



LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Ga-68	Gallium-68
IRB	Institutional Review Board
IV	Intravenous
PET/MRI	Positron emission tomography – magnetic resonance imaging
SUV	Standardized Uptake Value
GRPr	Gastrin releasing peptide receptor
BPH	Benign prostate hypertrophy
PSA	Prostate specific antigen
PSMA	Prostate specific membrane antigen

1. OBJECTIVE

1.1 Specific Aim

To evaluate ^{68}Ga-RM2 PET/MRI for detection of intermediate and high-risk prostate cancer prior to prostatectomy.

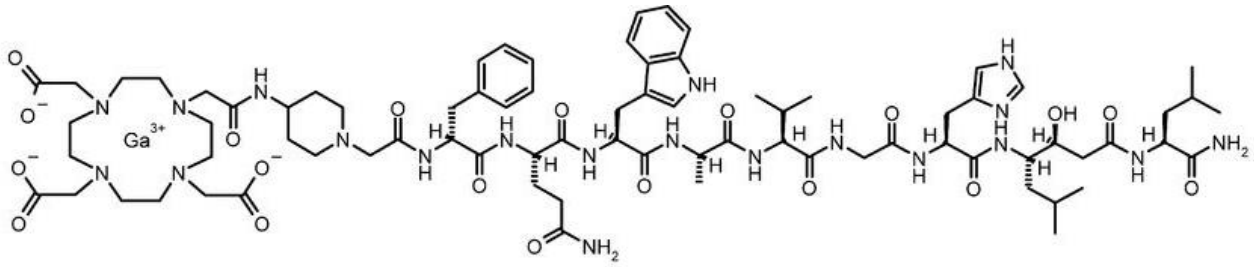


Figure 1. Chemical structure of ^{68}Ga-RM2

2. BACKGROUND AND SIGNIFICANCE

Data from the American Cancer Society suggests that for 2015 in the United States prostate cancer will continue to be the leading non-cutaneous cancer diagnosis in males with 220,800 estimated new cases, and has the second highest mortality (after lung) with 27,540 estimated deaths (*1*). Initial screening and diagnosis relies on the digital rectal exam (DRE), prostate specific antigen (PSA), and transrectal ultrasound-guided core biopsies (*2, 3*). Subsequent treatment is multifaceted and may involve observation, surgery (prostatectomy), radiation therapy (external beam or brachytherapy), hormonal therapy, chemotherapy, or a combination of these (*4-6*).

The choice of treatment directly depends on the initial staging, as well as the patient's age, co-morbidities, and preferences. Prostate cancer staging is based on the tumor-node-metastases (TNM) classification. As outlined in the National Comprehensive Cancer Network guidelines, those patients requiring staging for additional therapy would need a bone scan and pelvic CT or MRI if the T-stage is greater than 2 or if the PSA or Gleason score is elevated (> 20 ng/mL and > 8, respectively). The CT or MRI is primarily used to identify locoregional lymph nodes (thereby altering the N-stage), while the bone scan is primarily used to identify osseous metastatic disease (thereby altering the M-stage). In particular, the prognostic importance of bone metastases in patients with prostate cancer has been established. Patients with an abnormal bone scan at the time of diagnosis have a mortality rate twice as high as patients with normal bone scans (*7*).

However, at initial staging the issue is detection of pelvic and retroperitoneal small lymph node metastases that don't trigger size criteria on CT and MRI; bone metastases are a rare presentation.

Other tracers, such as ^{18}F- or ^{11}C-labeled choline and [^{11}C]-acetate, are used mainly for the diagnosis of recurrent (*8-10*) or metastatic (*11*) prostate cancer. Their feasibility in primary

diagnosis is limited because of uptake in benign tissue such as benign prostatic hyperplasia or inflammatory lymph nodes (*12, 13*).

Although choline based PET/CT is widely used outside the US for imaging prostate cancer, there have been numerous studies reporting a low sensitivity and specificity, especially at low prostate specific antigen (PSA) levels (*14, 15*). Consequently, improved imaging of prostate cancer is necessary. One novel promising method is PET imaging with ^{18}F-FACBC, a new synthetic amino acid. Recent evaluations by Nanni et al. indicate that this tracer might be superior when compared to choline PET/CT (*16*). However, recent work indicates that ^{18}F-FACBC uptake in prostate cancer is similar to that in BPH nodules (*17*). Prostate-specific membrane antigen (PSMA) continues to elicit high interest. This cell surface protein is significantly overexpressed in prostate cancer cells when compared to other PSMA-expressing tissues such as kidney, proximal small intestine or salivary glands. It therefore provides a promising target for prostate cancer-specific imaging. Recently methods have been developed to label PSMA ligands with ^{68}Ga and ^{18}F. Initial experience suggests that these novel tracers can detect prostate cancer relapses and metastases with high contrast by binding to the extracellular domain of PSMA, followed by internalization (*18, 19*). However, these promising agents do not detect all recurrences.

Consequently, improved imaging of prostate cancer continues to be an area of unmet clinical need. ^{68}Ga-labeled DOTA-4-amino-1-carboxymethyl-piperidine-D-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH2 (^{68}Ga-RM2, formerly also known as BAY86-7548 or ^{68}Ga-DOTA-Bombesin) is a synthetic bombesin receptor antagonist, which targets gastrin-releasing peptide receptors (GRPr) (*20*). GRPr proteins are highly overexpressed in several human tumors, including prostate cancer (*21*). Because of their low expression in BPH and inflammatory prostatic tissues (*22, 23*), imaging of GRPr has potential advantages over current choline- and acetate-based radiotracers. Indeed, preclinical studies using BAY86-7548 have shown a high and persistent tracer uptake in mice bearing PC-3 tumor xenografts, which represent androgen-independent human prostate cancer with high GRPr expression (*24*).

Clinicaltrials.gov

This study is registered on ClinicalTrials.gov as NCT03113617.

2.1 Rationale

In this study, we propose to use a well-established PET isotope, Gallium-68 (^{68}Ga), bound to a bombesin receptor antagonist, ^{68}Ga-RM2, which has high affinity for gastrin-releasing peptide receptors. GRPr proteins are highly overexpressed in several human tumors, including prostate cancer (*21*). Because of their low expression in BPH and inflammatory prostatic tissues (*22, 23*), imaging of GRPr has the potential to improve the lesion detection in prostate cancer. Therefore, we propose the following aim:

- To evaluate ^{68}Ga-RM2 PET/MRI for detection of intermediate and high-risk prostate cancer prior to prostatectomy

The first-in-human study investigated the safety, tolerability, metabolism, pharmacokinetics, biodistribution, and radiation dosimetry of ^{68}Ga-RM2. Five healthy men underwent dynamic whole-body PET/CT after an intravenous injection of ^{68}Ga-RM2 (138 ± 5 MBq). Besides total radioactivity, plasma samples were analyzed by radio–high-performance liquid chromatography for metabolism of the tracer. Dosimetry was calculated using the OLINDA/EXM software. The organs with the highest absorbed doses were the urinary bladder wall (0.62 mSv/MBq) and the pancreas (0.51 mSv/MBq). The mean effective dose was 0.051 mSv/MBq. ^{68}Ga-RM2 was well tolerated by all subjects. The authors concluded that the intravenously injected ^{68}Ga-RM2 is safe, and rapid metabolism is demonstrated. A 150-MBq injection of ^{68}Ga-RM2 results in an effective dose of 7.7 mSv, which could be reduced to 5.7 mSv with frequent bladder voids (*25*).

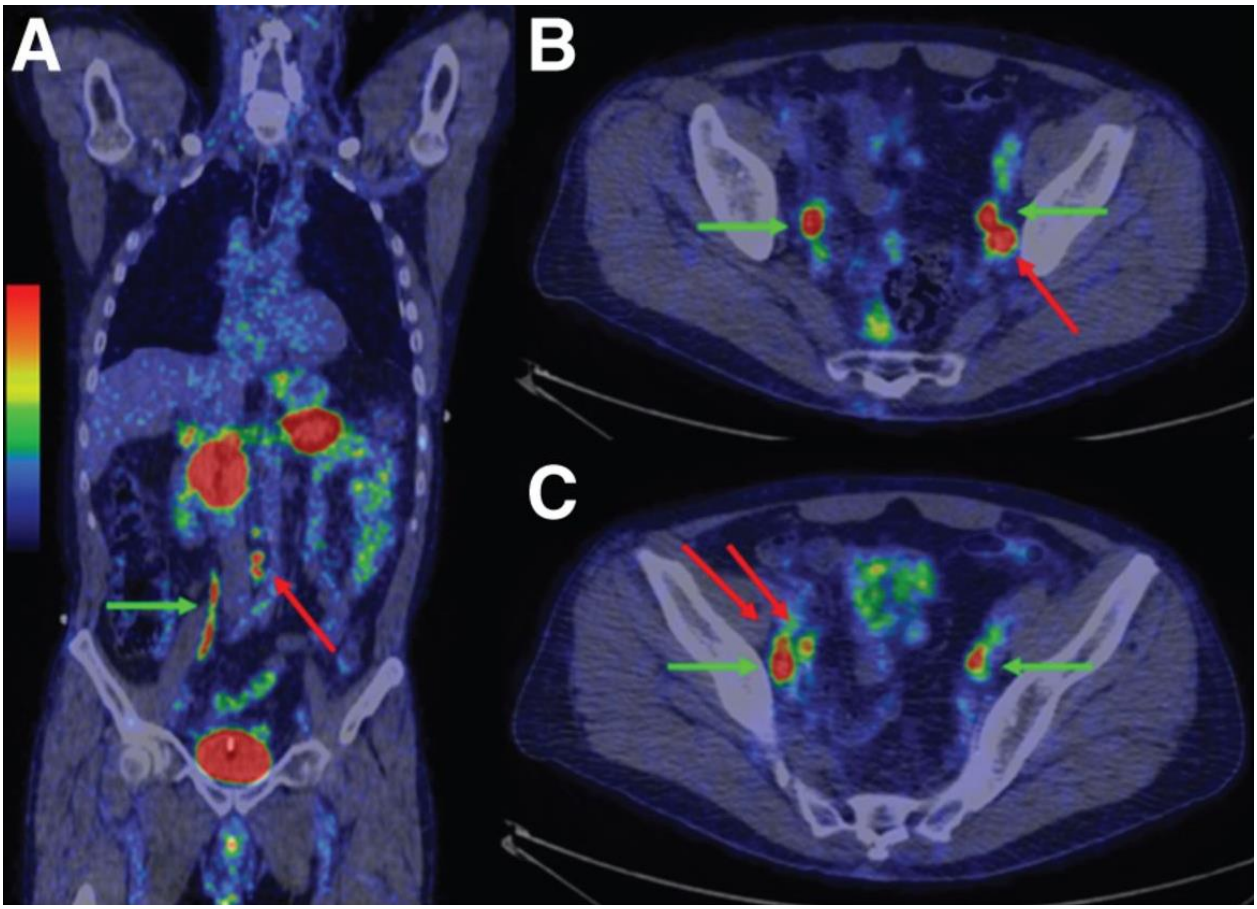


Figure 2: Coronal (A) and axial views (B and C) of ^{68}Ga-RM2 PET/CT in patient no. 8 with prostate cancer metastasis to multiple lymph nodes. Two normal-sized (less than 10 mm) nodes above the aortic bifurcation indicated with red arrow showed increased uptake of tracer, SUVmax 6.2 and 6.3. In addition, one left parailiac node, SUVmax 12.7, (B) and two right parailiac nodes, SUVmax 6.1 and 4.7, (C) showed increased uptake of ^{68}Ga-RM2. These five lymph nodes were histologically confirmed as metastases at surgery. Green arrows point to ureters, which can be easily distinguished on anatomic CT.

In the first study with ^{68}Ga-RM2 in patients with prostate cancer, 14 men scheduled for radical prostatectomy (n = 11) or with biochemical recurrence after surgery or hormonal therapy (n = 3) were enrolled. The patients received an intravenous injection of ^{68}Ga-RM2 followed by over 60-minute dynamic imaging of prostate gland (n = 10) and/or subsequent whole-body imaging (n = 14). The visual assessment of PET/CT images included evaluation of intraprostatic

(12 subsextants) and pelvic nodal uptake of ^{68}Ga-RM2 in 11 surgical patients and detection of potential metastatic foci in all patients. In patients with biochemical recurrence, results were compared with those of either ^{11}C-acetate (n = 2) or ^{18}F-fluoromethylcholine (n = 1) PET/CT. The authors reported a sensitivity, specificity, and accuracy of 88%, 81% and 83%, respectively, for detection of primary prostate cancer and sensitivity of 70% for metastatic lymph nodes using histology as gold standard (*26*). In our experience, ^{68}Ga-RM2 compared favorably against ^{68}Ga-PSMA (*27*).

2.2 Study Design

This is a prospective, single center, single-arm study enrolling 90 participants with intermediate and high-risk prostate cancer. Eligible participants will undergo baseline assessments at enrollment. Study participants will receive ^{68}Ga-RM2 and undergo a PET/MRI scan. All patients will first be seen by a Stanford Cancer Institute physician and then referred if appropriate on clinical grounds to Dr. Iagaru or his colleagues for this study. The following steps will take place.

1. After signed the informed consent document, participants will be given a copy of the signed form
2. Participant will be asked to drink 1 to 2 glasses of water before arrival at the clinic
3. Participants will be weighed and vital signs (heart rate and blood pressure) will be recorded
4. Study personnel (eg, technologist) will verify subject identify; radiopharmaceutical identity; dose; and administration route. Participant will be injected IV with 140 MBq ± 20% of ^{68}Ga-RM2
5. Participant will void immediately prior to the scan
6. Approximately 50 to 100 minutes after the radiopharmaceutical IV administration, data acquisition will begin in the pelvic region and move toward the head. First, localizer MRI scans will be performed to define the table positions. After correct positioning of the spatial acquisition windows is ensured, the combined PET/MRI acquisition will be initiated with 3 to 5 table positions at a 4-min acquisition time per table position.
7. Vital signs (heart rate and blood pressure) will be recorded again at the completion of the study.
8. Participants will be dismissed.
9. Participants will be contacted at 24 to 72 hours following the scan in order to capture potential late occurring Adverse Events.

The ^{68}Ga-RM2 PET/MRI may be repeated at the completion of treatment to evaluate response to therapy, if requested by the treating physician.

3. PARTICIPANT SELECTION AND ENROLLMENT PROCEDURES

3.1 Inclusion Criteria

- Older than 18 year-old
- Biopsy proven prostate adenocarcinoma
- Planned prostatectomy with lymph node dissection
- Intermediate to high-risk disease (as determined by elevated PSA [PSA>10], T-stage [T2b or greater], Gleason score [Gleason score > 6] or other risk factors)
- Able to provide written consent
- Karnofsky performance status of ≥50 (or ECOG/WHO equivalent)
- Diagnostic CT or MRI performed within 30 days prior to the ^{68}Ga-RM2 PET

3.2 Exclusion Criteria

- Inability to lie still for the entire imaging time (approximately 30 minutes)
- Inability to complete the needed investigational and standard-of-care imaging examinations due to other reasons (severe claustrophobia, radiation phobia, etc.)
- Any additional medical condition, serious intercurrent illness, or other extenuating circumstance that, in the opinion of the Investigator, may significantly interfere with study compliance
- Metallic implants (contraindicated for MRI)

3.3 Informed Consent Process

All participants will be provided a consent form describing the study with sufficient information for participants to make an informed decision regarding their participation. Participants must sign the IRB approved informed consent prior to participation in any study specific procedure. The participant must receive a copy of the signed and dated consent document. The original signed copy of the consent document must be retained in the medical record or research file.

3.4 Study Timeline

3.4.1 Primary Completion:

The study will reach primary completion 36 months from the time the study opens to accrual.

3.4.2 Study Completion:

The study will reach study completion 48 months from the time the study opens to accrual.

4. IMAGING AGENT INFORMATION

4.1 Study Agent

We will use ^{68}Ga-RM2 as the PET radiopharmaceutical. The administered dosage is 140 MBq ± 20% i.v.

4.2 Specify the source of the study agent

Molecular Imaging Program at Stanford
Satellite Radiochemistry Facility
300 Pasteur Dr, [redacted]
Stanford, CA 94305

4.3 Describe how the agent will be requested and provide mailing address and phone number.

Ordered in Radiology Information System (RIS), address per above.

4.4 Agent Accountability

RIS is password protected and part of the electronic medical records.

5. IMAGING SPECIFICS

5.1 Modality or Modalities to be used

PET/MRI

5.2 Details of Imaging (i.e. dynamic, static, number of scans, etc.)

We will use ^{68}Ga-RM2 as the PET radiopharmaceutical. The administered dosage is 140 MBq ± 20% i.v.

A localizer MRI scan will be performed at 45 minutes after injection of 140 MBq ± 20% of ^{68}Ga-RM2 to define the table positions. After correct positioning of the spatial acquisition windows is ensured, the combined PET/MRI acquisition will be initiated with 3 to 5 table positions at a 4-min acquisition time per table position. A volumetric T1 acquisition with fat-water separation and motion correction to enable free-breathing will be obtained at each table position and used for the generation of attenuation maps and for anatomic allocation of the PET results. Simultaneously with the start of the T1 MRI sequence, the PET acquisition will start at the same table position, thus ensuring optimal temporal and regional correspondence between MRI and PET data. The PET acquisition time will be 4 min per table position, taking delayed acquisition times and radioactive decay into account. As the T1 will take less than 4 minutes, a rapid diffusion weighted MRI will also be performed. After completion of the PET acquisition, the table will be moved to the next table position and the procedure will be repeated. Upon completion of the PET acquisition for all stations, volumetric post-contrast T1- and T2-weighted MR images may be obtained at multiple stations as needed.

The PET emission scan is corrected using segmented attenuation data of the MRI scan. The PET images are reconstructed with a standard iterative algorithm. All images are reformatted into axial, coronal, and sagittal views and viewed with the software provided by the manufacturer (AW, GE Medical Systems).

6. STUDY PROCEDURES

6.1 Criteria for Removal from Study

The Protocol Director may withdraw subjects from the study for one or more of the following reasons: failure to follow the instructions of the Protocol Director and/or study staff; determination that continuing the participation could be harmful to the subject; the study is cancelled or other administrative reasons.

6.2 Alternatives

The alternative is to not participate in the study.

7. STUDY CALENDAR

	Pre-Study	Week 1	24 - 72 Hours Post-Study	12 Months
Informed consent	X			
Demographics	X			
Medical history	X			
Follow-up Call to Participant			X	
^{68}Ga-RM2 PET/MRI		X		
Data analysis				X

8. ADVERSE EVENT REPORTING

We do not anticipate hazardous situations for the subjects as a result of this protocol. However, procedures will be in place for verification of correct radiopharmaceutical dose and route of administration (i.e., each dose will be double checked for dosimetry and quality by a researcher and technologist). The study Principal Investigator (PI) or his designee will report unanticipated AEs related to the Stanford CCTO Safety Coordinator within 10 working days of becoming aware of the event (5 days if the event is life-threatening or resulted in death) using the Adverse Events Communication Form. If the principal investigator determines the unanticipated adverse device effect presents an unreasonable risk to subjects, the study will be terminated as soon as possible, but no later than 5 working days after the PI makes the determination and no later than 15 working days after first receiving notification of the effect.

9. REGULATORY CONSIDERATIONS

9.1 Institutional Review of Protocol

The protocol, the proposed informed consent and all forms of participant information related to the study (e.g. advertisements used to recruit participants) will be reviewed and approved by the Stanford IRB. Any changes made to the protocol will be submitted as a modification and will be approved by the IRB prior to implementation. The Protocol Director will disseminate the protocol amendment information to all participating investigators.

9.2 Data Management Plan

The Stanford Cancer Institute Data and Safety Monitoring Committee (DSMC) will audit study related activities to determine whether the study has been conducted in accordance with the protocol, local standard operating procedures, FDA regulations, and Good Clinical Practice (GCP). This may include review of regulatory binders, case report forms, eligibility checklists, and source documents. In addition, the DSMC will regularly review serious adverse events and protocol deviations associated with the research to ensure the protection of human subjects. Results of DSMC audits will be communicated to the IRB and the appropriate regulatory authorities at the time of continuing review, or in an expedited fashion, as needed.

10. MEASUREMENTS

10.1 Study Endpoints

10.1.1 Primary endpoint:

i. Sensitivity, specificity, positive and negative predictive value of ^{68}Ga-RM2 PET for the detection of regional nodal metastases compared to pathology at radical prostatectomy on a per patient basis.

10.1.2 Secondary endpoint:

i. Sensitivity, specificity, negative and positive predictive value for detection of regional nodal metastases in comparison to cross sectional imaging performed contemporaneously with the ^{68}Ga-RM2 PET.

10.1.3 Exploratory endpoint:

i. One year PSA progression free survival, comparing patients with and without pelvic nodal metastases.

ii. Correlation between SUV_{max} from ^{68}Ga-RM2 PET and short axis diameter of nodal disease on cross sectional imaging correlate to presence of true pathology.

iii. Incidence of osseous and distant metastatic lesions.

10.2 Image interpretation:

10.2.1 ^{68}Ga-RM2 PET/MRI:

The PET/MRI scans will be interpreted by ABNM certified Nuclear Medicine physicians and ABR-certified radiologists. Consensus read will be obtained for each scan. Each lesion will be tabulated and a comparison of lesion detection by each scanner will be conducted.

Visual interpretation of PET data:

Regions of suspected disease will be graded on a two-point scale by each reader (0 = Negative or 1 = Positive). A region will be judged as positive if at least one lesion in this region is visually positive.

i. Lymph nodes will be considered positive if the ^{68}Ga-RM2 uptake is focal and greater than adjacent background. Pelvic lymph nodes will be sub-classified according to their localization as follows: R/L obturator, R/L external iliac, R/L internal iliac and other (total of 7 subgroups).

ii. Visceral lesions will be considered positive if the ^{68}Ga-RM2 uptake is focal and greater than physiologic background activity of the involvement organ or anatomic site.

iii. Bone lesions will be considered positive if the ^{68}Ga-RM2 uptake is focal and greater than physiologic bone marrow.

10.3 Follow-up:

a. Prostatectomy: patients without evidence of ^{68}Ga-RM2 PET positive nodal or metastatic disease noted on imaging will undergo radical prostatectomy. If a ^{68}Ga-RM2 PET positive regional pelvic node is noted, the urologist will be informed of the location of the suspicious node and the patient will undergo prostatectomy with nodal dissection.

   i. Patients with nodes seen on ^{68}Ga-RM2 PET without positive nodes on pathology, will be rescanned with MRI or CT to determine if the suspicious node was thought to be removed. A ^{68}Ga-RM2 PET may be repeated as well.

b. If sites of ^{68}Ga-RM2 PET positive osseous or distant metastatic lesions are noted, the urologist will be informed, and further evaluation including further imaging (bone scan, ^{18}F NaF PET, CT or MRI cross section imaging) or targeted biopsy will be performed in order to restage the patient prior to the decision regarding whether or not a prostatectomy will be performed as per the responsible surgeon and standard of clinical care.

c. The results of this research scan will be provided to the treating physician who may, at their discretion, decide to conduct further imaging scans and/or biopsies. The type and details of these additional scans are not specified, and are at the treating physician's discretion.

d. Pathology: Specimens from prostatectomy will be evaluated for the presence of nodal metastasis. This will be reported on a per patient basis as positive or negative.

   i. If possible, the presence of nodal disease on a per region basis (inguinal, left/right obturator, external and internal iliac, paraaortic nodal regions) should be performed. This data will be grouped for subanalysis.

   ii. The number of nodes counted on pathology will also be recorded.

10.4 Statistical analysis:

a. Sample size: 90 patients in total. The power analysis is based on the comparison of sensitivity between conventional imaging and ^{68}Ga-RM2 PET.

   i. 30% of intermediate to high-risk patients have nodal metastases at prostatectomy.

ii. Conventional imaging has a 45% detection sensitivity for nodal metastases on a per patient basis (2).

iii. ^{68}Ga-RM2 PET has a 60% detection sensitivity for nodal metastases on a per patient basis.

b. Statistical analysis: The sensitivity, specificity, positive and negative predictive value of ^{68}Ga-RM2 PET for the detection on a per patient basis will be determined using the below criteria:

i. True positive patient:

1. ^{68}Ga-RM2 PET positive for regional nodes; pathology at prostatectomy positive for regional nodes.
2. ^{68}Ga-RM2 PET positive for regional nodes, pathology negative for regional nodes, imaging after prostatectomy demonstrates node was not removed at surgery, and follow-up biopsy or imaging demonstrates presence of nodal disease.
    a. Criteria for positive node on follow-up imaging: imaging within 3-12 months, the node decreases by more than 30% (for patients undergoing systemic treatment or focal therapy at this site) or increase by more than 20% in short axis diameter in the absence of treatment (with a minimum of 3 mm in change in size).

ii. True negative patient:

1. ^{68}Ga-RM2 PET negative for regional nodes; pathology at prostatectomy negative for regional nodes.

iii. False positive patient:

1. ^{68}Ga-RM2 PET positive for regional nodes, pathology at prostatectomy is negative, and imaging after prostatectomy demonstrates that node is no longer present.

iv. False negative patient:

1. ^{68}Ga-RM2 PET negative for regional nodes, but pathology at prostatectomy is positive.

v. Non-evaluable:

1. ^{68}Ga-RM2 PET positive for regional nodes, pathology negative for regional nodes, imaging after prostatectomy demonstrates node was not removed at surgery, and no definitive follow-up is available.
2. Patients with extrapelvic nodal metastases will not be included in this analysis if patients do not undergo prostatectomy.

11. ADVERSE EVENTS AND REPORTING PROCEDURES

11.1 Potential Adverse Events

The administration of the radioactive substance will feel like a slight pinprick when given by i.v. injection. Patients who are claustrophobic may feel some anxiety while positioned in the

scanner. Also, some patients find it uncomfortable to hold one position for more than a few minutes. The subjects will not feel anything related to the radioactivity of the substance in their body. Because the radioactivity is very short-lived, the radiation exposure is low. The substance amount is so small that it does not affect the normal processes of the body.

This research study involves exposure to radiation. This radiation exposure is for research purposes only. The amount of radiation from one ^{68}Ga-RM2 PET is 4.76 mSv, approximately equal to 10% of the limit that radiation workers (for example, a hospital x-ray technician) are allowed to receive in one year. There is no radiation exposure from MRI. Therefore, the total radiation exposure is 4.76 mSv. This amount of radiation involves minimal risk and is necessary to obtain the research information desired.

Appendix: Inclusion/Exclusion Criteria Checklist

Protocol Title:	^{68}Ga-RM2 PET/MRI for Detection of Regional Nodal and Distant Metastases in Patients with Intermediate and High-Risk Prostate Cancer
Protocol Number:	IRB-40373
Principal Investigator:	Andrei Iagaru, MD

Inclusion Criteria – "Yes" must be checked to be eligible (From IRB approved protocol)	**Yes**	**No**	**Supporting Documentation**
1. Older than 18 year-old	☐	☐	☐
2. Biopsy proven prostate adenocarcinoma	☐	☐	☐
3. Planned prostatectomy with lymph node dissection	☐	☐	☐
4. Intermediate to high-risk disease (as determined by elevated PSA [PSA>10], T-stage [T2b or greater], Gleason score [Gleason score > 6] or other risk factors)	☐	☐	☐
5. Able to provide written consent	☐	☐	☐
6. Karnofsky performance status of ? 50 (or ECOG/WHO equivalent)	☐	☐	☐
7. Diagnostic CT or MRI performed within 90 days prior to ^{68}Ga-RM2 PET	☐	☐	☐

Exclusion Criteria – "No" must be checked to be eligible (From IRB approved protocol)	**Yes**	**No**	**Supporting Documentation**
1. Inability to lie still for the entire imaging time (approximately 30 minutes)	☐	☐	☐
2. Inability to complete the needed investigational and standard-of-care imaging examinations due to other reasons (severe claustrophobia, radiation phobia, etc.)	☐	☐	☐
3. Any additional medical condition, serious intercurrent illness, or other extenuating circumstance that, in the opinion of the Investigator, may significantly interfere with study compliance	☐	☐	☐
4. Metallic implants (contraindicated for MRI)	☐	☐	☐

*****All subject files must include supporting documentation to confirm subject eligibility. The method of confirmation can include, but is not limited to, laboratory test results, radiology test results, subject self-report, and medical record review.

i. Statement of Eligibility

By signing this form of this trial I verify that this subject is [☐**eligible** / ☐ **ineligible**] for participation in the study. This study is approved by the Stanford Cancer Institute Scientific Review Committee, the Stanford IRB, and has finalized financial and contractual agreements as required by Stanford School of Medicine's Research Management Group.

Treating Physician Signature:	Date:
Printed Name:	

Secondary Reviewer Signature:	Date:
Printed Name:	

Study Coordinator Signature:	Date:
Printed Name:	

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