AWARD NUMBER: W81XWH-16-1-0604

TITLE: 68Ga Bombesin PET/MRI in Patients with Biochemically Recurrent Prostate Cancer and Noncontributory Conventional Imaging

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Stanford, CA 94305

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Fort Detrick, Maryland 21702-5012

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Purpose: $^{68}$Ga-labeled DOTA-4-amino-1-carboxymethyl-piperidine-D-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH$_2$ ($^{68}$Ga-RM2) is a synthetic bombesin receptor antagonist that targets gastrin-releasing peptide receptors (GRPr). GRPr proteins are highly overexpressed in several human tumors, including prostate cancer (PCA).

Methods: We enrolled 15 men with biochemically recurrent PCAs from May to Sep 2017, 63-79 year-old (mean±standard deviation (SD): 70.3±4.3). Imaging started at 41-89 minutes (mean±SD: 53.6±14.1) after injection of 127.5-146.5 MBq (mean±SD: 141.0±4.7) of $^{68}$Ga-RM2 using a time-of-flight (TOF)-enabled simultaneous positron emission tomography (PET)/magnetic resonance imaging (MRI) scanner. T1-weighted (T1w), T2-weighted (T2w) and diffusion-weighted images (DWI) were acquired.

Results: All patients had rising prostate specific antigen (PSA) (range: 0.2 -12.5 ng/mL; mean±SD: 4.2±4.4) and negative CI (CT or MRI, and $^{99m}$Tc MDP bone scan) prior to enrollment. The observed $^{68}$Ga-RM2 PET detection rate was 73.3%. $^{68}$Ga-RM2 PET identified recurrent PCA in 11 of the 15 participants.

Conclusions: $^{68}$Ga-RM2 PET can be used for assessment of GRPr expression in patients with biochemically recurrent PCAs. High uptake in multiple areas compatible with cancer lesions suggests that $^{68}$Ga-RM2 is a promising PET radiopharmaceutical for localization of disease in participants with biochemically recurrent PCAs and negative conventional imaging.

15. SUBJECT TERMS
Prostate cancer, Bombesin, PET, PET/MRI, clinical research, receptors
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INTRODUCTION

Prostate cancer (PCa) is the most common malignancy in elderly men (1) and the second leading cause of cancer death after lung and bronchus tumors (2). Up to 40% of prostate cancer patients develop biochemical recurrence within 10 years after radical treatments (3) and morphological imaging methods exhibit considerable limitations in detecting relapsed disease early (4). Gastrin releasing peptide receptors (GRPr), part of the bombesin (BBN) family, are overexpressed in several human tumors including prostate cancer.

Combined positron emission tomography (PET) and magnetic resonance imaging (MRI) targeting the GRPr with a $^{68}$Ga-labelled bombesin analog receptor antagonist (RM2) is used as a promising diagnostic method for patients with suspicion of PCa recurrence. Here, we evaluate the role of $^{68}$Ga-RM2 PET/MRI in patients with biochemical recurrence of PCa and negative conventional imaging.

The main goal of our study is to evaluate if $^{68}$Ga-RM2 PET/MRI can improve the diagnostic accuracy of recurrent prostate cancer earlier, when PSA level is still low and no disease is seen by conventional imaging. This would lead to timely and more accurate treatments with impact on overall survival and quality of life.

References:


KEYWORDS

Prostate cancer, bombesin, $^{68}$Ga, RM2, PET, PET/MRI, clinical research, receptors

ACCOMPLISHMENTS

Major goals of the project

<table>
<thead>
<tr>
<th>Specific Aim 1 (specified in Project Narrative)</th>
<th>Original Timeline</th>
<th>Progress</th>
<th>Date Completed</th>
</tr>
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<tbody>
<tr>
<td>To compare the diagnostic performance of $^{68}$Ga-RM2 PET/MRI to that of conventional imaging (CI) for detecting recurrent prostate cancer.</td>
<td>Months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time needed to get protocol approved by HRPO</td>
<td>1-5</td>
<td>100%</td>
<td>03/20/17</td>
</tr>
<tr>
<td>Prepare to start enrollment of participants</td>
<td>1-2</td>
<td>100%</td>
<td>05/01/17</td>
</tr>
<tr>
<td>Enroll participants</td>
<td>Ongoing</td>
<td>15%</td>
<td>Ongoing</td>
</tr>
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</table>
Accomplishments under goals

1) **Major activities:*** enrolling eligible patients and reviewing $^{68}$Ga-RM2 PET/MRI images to investigate its role as stated in #2.

   We enrolled 15 participants in the Jun-Sep 2017 time frame. June is effectively the start date for enrollment since we needed time for HRPO approval and to run validation runs locally afterwards. At this accrual rate (>4 enrolled each month) we are on target for complete and timely accrual.

2) **Specific objectives:** The specific objectives of the goals included: obtaining study approvals from the Stanford Institutional Review Board and the DOD CDMRP HRPO, designing the clinical database, enrolling eligible patients, performing $^{68}$Ga PET/MRI of the eligible patients, review images.

   All of the above have been completed or are in progress, as detailed in #1.

3) **Significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative):**

   $^{68}$Ga-RM2 PET/MRI was able to detect findings compatible with prostate cancer recurrence in 11 of the 15 participants enrolled to date. There were no failures in $^{68}$Ga-RM2 synthesis, scanner operation or otherwise.

4) **Stated goals not met:**

   None

Opportunities for training and professional development

We hired a research fellow as specified in the submission. In addition, in the Division of Nuclear Medicine and Molecular Imaging are assisting with the enrollment of eligible participants and collecting and analyzing data, respectively. This is an excellent opportunity for them to learn about clinical research.

Results disseminated to communities of interest

$^{68}$Ga-RM2 PET/MRI is promising for improving the diagnostic accuracy in patients with biochemical recurrence of prostate cancer and negative conventional imaging. We presented the results at local and regional meetings, including at a patient outreach event organized by Stanford HealthCare. We plan to continue to present results at local, national and international meeting in order to disseminate results to communities of interest.

Plans for next reporting period to accomplish goals

We plan to closely monitor study enrollment, with the goal of enrolling 2-3 patients a month in order to meet the study recruitment goal of 100 participants overall. If the study recruitment goals are met early, we will make every attempt to complete the project in a timely manner and expedite efforts where we can.
IMPACT

Impact on the development of the principal discipline(s) of the project
Nothing to report

Impact on other disciplines
Nothing to report

Impact on technology transfer
Nothing to report

Impact on society beyond science and technology
Nothing to report
CHANGES/PROBLEMS

Changes in approach and reasons for change
Nothing to report

Actual or anticipated problems or delays and actions or plans to resolve them
Nothing to report

Changes that had a significant impact on expenditures
Nothing to report

Significant changes in use or care of human subjects
Nothing to report

Significant changes in use or care of vertebrate animals
Nothing to report

Significant changes in use of biohazards, and/or select agents
Nothing to report

PRODUCTS

Journal publications
Nothing to report

Books or other non-periodical, one-time publications
Nothing to report

Other publications, conference papers, and presentations
Nothing to report

Website(s) or other Internet site(s)
Nothing to report

Technologies or techniques
Nothing to report
### Inventions, patent applications, and/or licenses

Nothing to report

### Other products

Nothing to report

## PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

### Individuals who have worked on the project

<table>
<thead>
<tr>
<th>Name</th>
<th>Project Role</th>
<th>Nearest person month worked</th>
<th>Contribution to project</th>
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</thead>
<tbody>
<tr>
<td>Iagaru, Andrei Horia</td>
<td>Principal Investigator</td>
<td>1</td>
<td>Dr. Iagaru has worked with all personnel to oversee the project (no change)</td>
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<tr>
<td>Brooks, James Duane</td>
<td>Co-Investigator</td>
<td>&lt;1</td>
<td>Dr. Brooks has assisted with participants referrals</td>
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<tr>
<td>Loening, Andreas Markus</td>
<td>Co-Investigator</td>
<td>&lt;1</td>
<td>Dr. Loening has assisted with analysis of MRI data</td>
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<tr>
<td>Mittra, Erik S</td>
<td>Co-Investigator</td>
<td>&lt;1</td>
<td>Dr. Mittra has assisted with analysis of PET data</td>
</tr>
<tr>
<td>Srinivas, Sandhya</td>
<td>Co-Investigator</td>
<td>&lt;1</td>
<td>Dr. Srinivas has assisted with coordinating the clinical study</td>
</tr>
<tr>
<td>Vasanawala, Shreyas Shreenivas</td>
<td>Co-Investigator</td>
<td>&lt;1</td>
<td>Dr. Vasanawala has assisted with analysis of MRI data</td>
</tr>
<tr>
<td>Name:</td>
<td>Baratto, Lucia</td>
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<tr>
<td>Project Role:</td>
<td>Clinical Postdoctoral Fellow</td>
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<td>Nearest person month worked:</td>
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<tr>
<td>Contribution to project:</td>
<td>Dr. Baratto has assisted with patient enrollment and consenting, data collection and analysis.</td>
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<th>Name:</th>
<th>Rosenberg, Jarrett</th>
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<tr>
<td>Project Role:</td>
<td>Statistician</td>
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<td>Nearest person month worked:</td>
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<td>Contribution to project:</td>
<td>Dr. Rosenberg has assisted with data analysis.</td>
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<tr>
<th>Name:</th>
<th>Jordan Cisneros</th>
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<tr>
<td>Project Role:</td>
<td>Research Coordinator</td>
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<tr>
<td>Nearest person month worked:</td>
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<td>Contribution to project:</td>
<td>Jordan Cisneros has assisted with patient recruitment and scheduling.</td>
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Changes in active other support of the PD/PI(s) or senior/key personnel since the last reporting period
Nothing to declare

Other organizations involved as partners
Nothing to report

Location of organization:
Partners contribution to the project:

SPECIAL REPORTING REQUIREMENTS
Nothing to report

APPENDICES
Nothing to report